REFLEX VASODILATATION OF THE FINGERS IN THE STUDY OF PERIPHERAL VASCULAR DISORDERS

With special reference to diabetes mellitus

BY

KJELL SIGROTH

GÖTEBORG 1957

FROM THE MEDICAL CLINIC I, SAHLGRENSKA SJUKHUSET, UNIVERSITY OF GÖTEBORG, THE MEDICAL DEPARTMENT OF LÄNSLASARETTET, MÖLNDAL, AND THE DEPARTMENT OF CLINICAL PHYSIOLOGY, SAHLGRENSKA SJUKHUSET, UNIVERSITY OF GÖTEBORG

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Introduction

During the past twenty-five years the clinical study of peripheral vascular disorders has gained increasing interest. More and more complicated methods have been introduced in the study of peripheral circulation. The technically advanced, time-consuming and expensive methods, necessary for determining the blood flow in different parts of the periphery of the body, have caused a tendency to concentrate clinical investigations on vascular disorders to more or less specialized vascular clinics. At the same time there is a risk of the diagnostics in this field of medicine being neglected at other clinics. To prevent such a development there is a need of simple methods which can be adopted at every hospital.

One of these simple procedures is the measurement of skin temperature. Introduced as a clinical method by Ipsen in 1917 (1936), it has been widely spread in the diagnostics of peripheral vascular disorders. As the skin temperature is not proportional to the blood flow on all conditions (Fetcher, Hall & Shaub 1949, Hensel 1952) the use of skin temperatures in diagnostic work has been criticized (Hensel 1952, 1956). The accordance between skin blood flow and skin temperature has been rather good when the blood flow is steady (Felder, Russ, Montgomery & Horwitz 1954) or increasing, but less reliable during a decrease of flow (Burton 1939). Many investigators have not percieved this condition of things, their results have been contradictory and the skin temperature measurements judged as useless in clinical work.

The blood flow in the skin can be kept steady or almost steady at maximal constriction or dilatation of the vessels without much expenditure of time and technical equipment. If the peripheral circulation is studied under other circumstances than at maximal vasoconstriction or dilatation a constant skin blood flow cannot be expected unless the examination is performed after a long period of adaptation.

In recent times most clinical investigators on peripheral circulation have preferred to measure the blood flow either during an increase or after the dilatation has been considered as complete. Several methods have been employed to provoke vasodilation. Surveys of these methods are found in the textbooks of Allen, Barker & Hines (1955), Samuels (1956), Martin & al. (1956) and Abramson (1956). A critical survey was given by Brattgård, Lindqvist & Sigroth (1951) concluding that a hot bath of 42—44 °C on suitable conditions always produced a complete vasodilatation in the feet of healthy

subjects, and that this procedure was not injurious to the patient. The induction of vasodilatation in some part of the body through heating some other part has been called *reflex* or indirect *vasodilatation* (see Terminology).

Since 1947, I have worked with problems on peripheral vascular disease. My interest previously was mainly directed to the circulation of the feet (Brattgård et al. 1951, Lindqvist & Sigroth 1952, Lindqvist, Sigroth & Blomberg 1957). In the first of these studies an attempt was made to standardize the conditions of the reflex dilatation of the toes. The proceeding of the vasodilatation in the toes of healthy subjects was followed by skin temperature measurements. The limits were calculated for the variation of the temperature curves. In the two last papers the clinical diagnostic applicability of these experiments was demonstrated, and the advantage of measuring all toes simultaneously was emphasized.

In these earlier investigations the experimental conditions were selected more according to clinical experience and results of other investigators than systematical analysis of the factors which might influence the results. The control material was also rather limited and did not cover the possible variations in sex and age of material of patients with vascular disorders.

The present investigation was planned to establish a similar basis of control results to the application of reflex vasodilation as a clinical method in the diagnostics of vascular disorders of the hands. A larger variance in the age and sex distribution of the control subjects was pursued to permit the deduction of possible systematic variations.

The influence of the experimental conditions on the results of the examinations was also investigated, especially the temperature and humidity of the room. If it were necessary to have an air conditioned room for the examinations these could not be performed at every hospital.

The results obtained in the control material during standardized conditions were used for calculating the limits of variation in temperature curves compatible with an unimpaired finger circulation.

Some materials of patients with various disorders were also investigated in the same manner, and the results compared to those of the control group.

Patients with high or low basal metabolic rate (BMR) were examined in order to establish the effect of BMR on the examination results.

Patients with various vascular disorders of the fingers were examined to investigate the value of the present procedure in diagnostic work as compared to other methods of clinical investigation used at such disorders.

A material of diabetic patients was also examined. Patients of various age and duration of disease were selected. Some of them could be expected to have signs of vascular impairment of the fingers because of their suffering from diabetic complications in spite of their lack of symptoms indicating vascular disorders. The occurrence of pathological vascular reactions was

placed in relation to other signs and complications of the diabetic disease in order to evaluate the influence of these factors in the origin of the pathological vascular reactions.

It is evident from the present work that skin temperature measurements in the diagnostics of peripheral vascular disease are valuable. This statement would be impossible unless the thorough and time-consuming penetration of the temperature curves in control subjects and patients with vascular disease had been performed. It can be expected that the method can be simplified for practical use after this extensive investigation without neglecting the reliability. It is my hope that this simple method may be helpful in the study of the immense material of peripheral vascular disorders.

Terminology

The monograph »Peripheral vascular diseases» by Allen, Barker & Hines (1955) begins with a chapter on definitions of terms. These definitions have been followed with some exceptions.

As pointed out by these authors some of the terms are not adequate, and should be discarded, but time and usage have given them respectability. Many of these terms have been avoided, as far as possible, in the present work, but sometimes they must be used in the discussions of references and to escape unnecessary enumerations.

The principal method of the present work i. e. the warming of the hands by heating the feet is, thus, called *reflex vasodilatation*. This term is also used by Goetz (1956) while Abramson (1956) prefers the term »indirect vasodilation» for the same phenomenon and Lynn (1956) »indirect body heating».

The term *peripheral vascular disorders* has been used to represent all deviations of the peripheral circulation from that generally seen.

Peripheral vascular disease is defined as the condition where the patient has symptoms or signs of disease in the blood vessels outside of the heart and where no generally accepted cause of the disease is to be found in the vessels additionally.

According to Werkö (1955) heart insufficiency is defined as insufficiency of circulation, appearing in different cardiac diseases, and depending on the incapacity of the heart in fulfilling its task as a pump.

In the statistical considerations S. D. denotes the standard deviation and P the value of probability.

The Arabic numerals in brackets refer to the consecutive numbers of the control subjects. If a capital letter stands before the figures it refers to a series of patients.

Other terms used are defined in the following text.

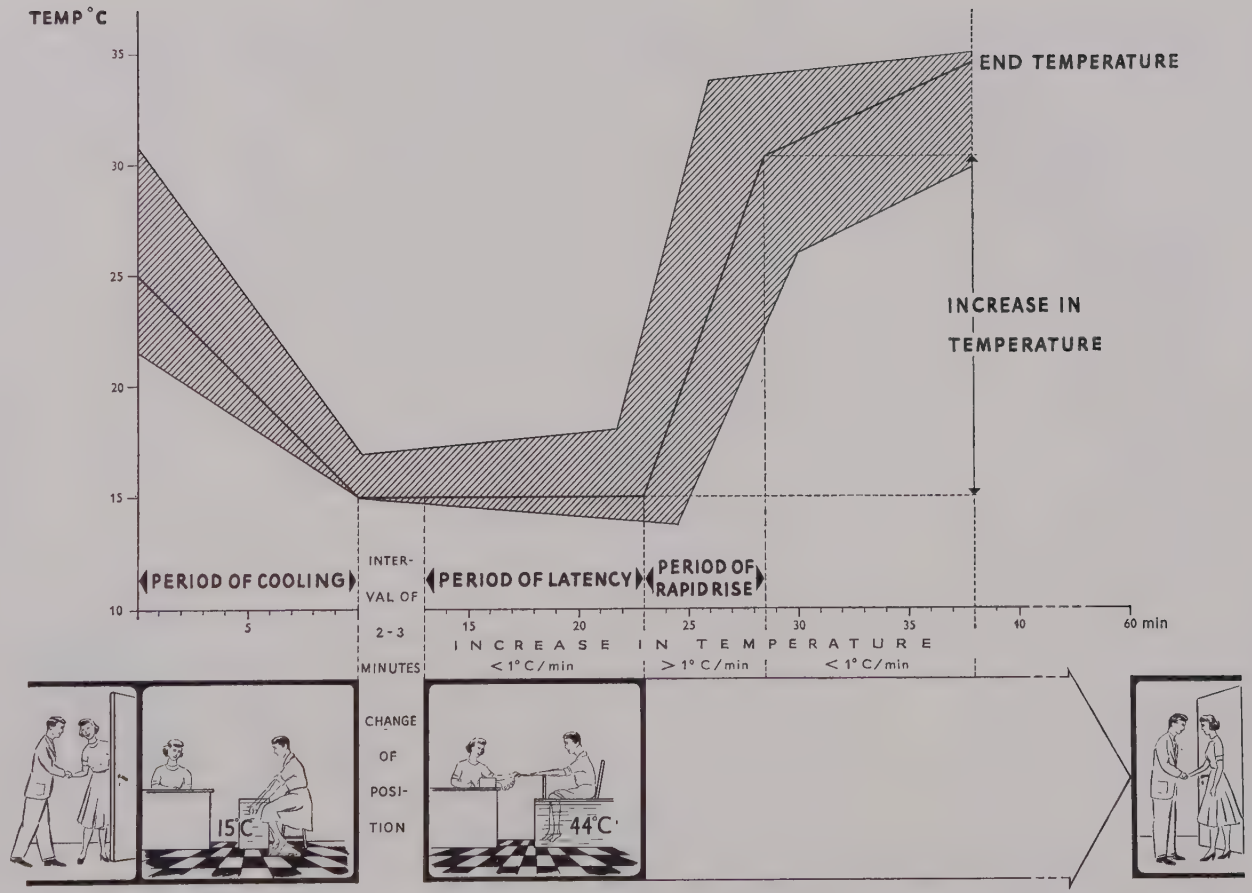


Figure 1. *The Course of the Examination.* The hatched area approximately corresponds to the variations in the courses of temperature curves observed in control subjects. The dispersion of the periods of latency, however, has intentionally been disregarded. The continuous line in this area marks the means of the variables. The pictures below the diagram illustrate the positions of the subject during the examination.

CHAPTER I

METHODS

A. Description of Own Methods

1. Survey of Methods

The principal method is a reflex vasodilatation controlled by skin temperature measurements. It is a modification of the method described by Gibbon & Landis (1932). The modification was designed by Lindqvist (1945) and is in principle the same as the method used in studying toes by Brattgård & al. (1951). (Figure 1.)

On arriving at the laboratory, either from the ward or from outside, the subject undressed all, except the closest underwear. After that he put on a bathrobe with the sleeves rolled to the elbows. Then he entered an air conditioned chamber with a constant air temperature, as a rule 15° C ± 1° C, and a relative humidity of about 50 per cent. The subject was placed on a low stool with his feet on a thick bath towel to prevent his feet from being inconveniently chilled. He rested his elbows on his knees with the flats of his hands facing the examiner. The hands were held at about the level of the heart. The measurements of the temperature were then started.

With gentle pressure the examiner placed the thermocouple to the center of the pulp of the right thumb, awaited the deflection of the galvanometer, and placed the thermocouple to the second right finger. While awaiting this deflection the result of the first finger was recorded. In that manner the measuring and the recording of the fingers proceeded to the right little finger, and after that on the left hand from the thumb to the little finger. This order of measuring was always followed. With some experience, the examiner is capable to perform all the ten measurings and notations in about 45 seconds. If the temperatures of all the fingers were not below 30° C the person to be examined was allowed to rest for a few minutes, after which a new series of measurements was performed. When the finger pulp temperatures were all below 30° C both the arms were immersed to the middle of the forearm in a container with water at a temperature of 15° C and the time of immersion was recorded. After 10 minutes in the water the hands were withdrawn and gently dried with a smooth towel and blotting paper until there was no moisture left on the surface. No rubbing was permitted.

Another measuring series was performed on the finger pulps. As a rule the temperatures noted were about that of the water or 1—2° C higher. Occasionally the temperatures of the pulps were still higher, especially in patients with increased metabolic rate. In such cases another period of cooling was employed.

After the hands had been sufficiently cooled, the subject was placed on a hard cover over a small bath. His legs were immersed through a hole in the cover in water of 43—44° C well above the middle of the calf. The hole was covered with a plastic cloth. The hands were placed at about the level of the heart on a board also covered with plastic cloth.

All these manipulations from the time the hands were removed from the cool water until the feet were put into the hot bath and the hands ready for further measurements did not, as a rule, last more than 3 minutes.

The finger measurements were now continued so that the temperatures of all the fingers were measured and recorded each minute. After some minutes the temperatures of the finger pulps generally increased, one after the other, or at the same time. In healthy persons there was mostly a slow rise in temperature for some minutes, followed by a rapid rise in a comparatively short time to about 30° C and after that another period of slower, undulating rise of temperature to about 33—35° C. The examination was then terminated.

In many patients, however, there were only slight signs of rise in temperature within 35 minutes or the pulp temperature did not exceed 32° C in a reasonable time. Then the examination was sometimes completed in two different ways: 1. ulnar nerve conduction anaesthesia at the elbow and 2. reactive hyperaemia produced by obstructing arterial circulation to the hand with a blood pressure cuff around the wrist for five minutes. During these procedures the heating of the legs was continued. The temperature readings were also continued some 10—20 minutes after the anaesthesia was developed, or the cuff was deflated in order to observe if there was any further rise in temperature induced by these manipulations.

2. The Laboratory

The laboratory is a square room with a floor area of about 2.5×2.5 meters and 3 meters between floor and ceiling. The walls are isolated with cork. The door has a draught-excluding braid. The ceiling is made of thick ligneous fiber board perforated with 2 mm holes every third cm. Above the ceiling there is an air conditioning equipment which gives the fresh air from outside a constant temperature and humidity and afterwards presses the air through the holes in the ceiling. The conditioned air is thus dispersed over the room. The air flows out through a ventilator in the ceiling preventing any draught. Fast cooling and heating of the room is arranged by an extra air channel in

one wall, allowing the air to pass freely from the air conditioning equipment to the room. The maximal air velocity has been 1 meter/second. The floor is made of artificial marble that isolates well and is easy to keep clean. The room is illuminated with an electric fluorescent tube that emits much light but little heat. In one of the walls there is a little window permitting the experiments to be supervised without entering the room.

The temperature of the room was controlled continuously by a mercury thermometer suspended in the middle of the room. In the present investigation the room temperature was kept at 15° C ($\pm$1° C). Other temperatures (18 and 20° C) were used, but only in control examinations to test if altered room temperatures had any influence on the examination results. The humidity was controlled on several occasions with a registering hygrometer and appeared to be very constant. It was kept at 50 per cent $\pm$5 per cent. The tempering and the humidity control has been very satisfactory, although, there sometimes were three adults and a bath filled with about 250 litres of water at 44° C heating the room.

The cooling of the fingers was performed in a container holding 40 litres of water. Ordinary 10 litre water buckets were tried, but the heat dissipating from the hands warmed these small amounts of water several degrees during the cooling time regularly used. Most authors who use water for cooling the skin recommend stirring the water to prevent a warm layer of water to be formed on the skin surface. For that reason the subjects were asked to move their hands gently in the water.

The legs were heated in a small bath containing about 250 litres of water. To prevent the heat of the bath from interfering with the air conditioning and the air of the room to cool the water, the bath was insulated. The insulation had to be light, so that the bath could be moved, but yet effective. For that reason a box suiting the bath was made of masonite. The inner surface of that box was foiled with smooth aluminium. The interspace between the bath and the box was filled with loosely creased strips of aluminium foil. The purpose of this foil insulation was to reflex and disperse the heat radiation with many smooth surfaces. At the same time the foil was too thin to conduct much heat, and the air in the space was prevented from circulating. The bath was also furnished with a cover of 15 mm wood, lacquered on both sides. The cover has an opening allowing sufficient space for the legs. The space between the legs and the border of the opening was covered with a manifold thin cloth of insulating plastic. There is no doubt that this upper surface of the bath was less insulated than the other ones. If the surface temperature of the insulated bath was measured, about half an hour after the bath had been filled with water of 44° C, the bottom and sides of the box had a temperature of approximately 17° C but the cover about 25° C. The cover, however, was almost taken up by the subject and his rather thick bath-robe so that

it was not considered necessary to improve the insulation. The subject got some extra heat applied to his back which might influence the vascular tone. The heat contribution, however, was the same for all the subjects and only made them more comfortable. The cover of the bath was furnished with a support for the back enabling the subject to relax during the examination. There was also a support for the hands at about the level of the heart.

The bath was filled with water of 44° C to cover the legs of the subject up to approximately 10 cm below the popliteal space. No stirring was used but the subject was asked to move his legs a little to prevent any layer of less warm water to form on the surface of the legs. No additional warm water was provided during the examination. The temperature of the bath dropped about 1° C/hour.

3. The Measuring Instrument

The construction of the electric skin thermometer used in the present investigation has been described by Leschly-Jacobsen (1956) but only in Danish.[1]) For that reason a recapitulation is given here.

It is a thermoelectric instrument where the measuring circuit is constructed of two wires, one of stainless steel and the other from constantan. These are fused at their ends in two junctions (thermocouples). One of these is the measuring junction and it has a surface of about 1—2 mm². It is mounted in an excavation in a pencilshaped holder of ebonite. The wires extend in free air only about 5 mm and the junction is situated above the centre of the cavity. The wires between the pencilshaped holder and the galvanometer run through a rubber-isolated cable.

The other — reference — junction between the wires is placed in a flute made in a metal block with great thermal capacity. This metal block adapts itself to the temperature of the room and is after that very resistant to the small fluctuations of temperature that may be expected in an ordinary laboratory.

The e. m. f. generated between the junctions is measured by a mirror galvanometer and may be read on a scale calibrated directly in centigrade; on the author's instrument beginning at 12° C and ending at 42° C. (The standard instrument has a scale ranging from 15°—45° C). The ultimate division of the scale is in 0.2° but 0.1° may easily be estimated. The galvanometer is adjusted to minor differences in the room temperature through a screw, regulating the torsion of the galvanometer filament.

A variation of the room temperature of 10° C will not displace the zero point of the galvanometer more than 0.1° C (Leschly-Jacobsen). As the room

[1]) The apparatus was manufactured by »Elektrolaboratoriet» in Copenhagen.

temperature was constant between the limits of $\pm 0.5^\circ$ C, the accuracy of the observations was not influenced. If, however, the apparatus must be moved from one laboratory to another with a different room temperature, it is safe to let the instrument adapt itself to the new room temperature for about an hour.

The measuring junctions are connected with the reference junction with connecting plugs. These plugs are made of the same metal as the corresponding wires, to avoid generation of false currents. One measuring junction may be exchanged for another with a switch where the conductive parts are also made in the same manner. Whenever the switch or plugs are used, however, there is an e. m. f. generated which brings the galvanometer circuit out of balance for about 30 seconds. For that reason the switch and the connecting plugs have not been touched during the experiments except for some special observations, dealt with later on.

As there were 400—1,200 temperature determinations in each experiment and about 600 experiments performed, there must be some wear of the measuring junctions. Five measuring junctions were used, all calibrated at the Institute of Electricity and Electrical Measurements at Chalmers University of Technology, Göteborg. The measuring thermocouples were almost equivalent. At 15° C they did not show more than 0.5° C higher temperature than a mercury thermometer and between 19° and 40° C the deviation was not more than $\pm 0.25^\circ$. As the accuracy of a thermoelectric skin surface measurement is not more than $\pm 0.5^\circ$ C according to several authors (Hardy 1934, Whyte 1951) this error was neglected in the calculations, especially as the calibrations were made in an oil bath and not in air in which medium the experimental measurements were performed.

Leschly-Jacobsen carried out his calibration in a water bath and found a deviation not exceeding $\pm 0.1^\circ$ C. I performed calibration curves to three of the measuring thermocouples in the water bath of a Hoeppler universal thermostat. At a room temperature of 21° C, which was about the same as that Leschly-Jacobsen used in his work, I found the deviation of the thermocouples from the mercury thermometer to be $\pm 0.1^\circ$ C. At a room temperature of 15° C in which most of the experiments of this work were done the deviation was $\pm 0.2^\circ$ C.

This instrument for measuring skin temperatures was theoretically well suited to give accurate results. As the galvanometer deflection of one measurement was generally completed in less than 5 seconds, and as my observations were done on several points successively within one minute, the thermocouple would never give any insulation to the skin from the surrounding air.

The wires of steel and constantan are too thin to conduct any considerable heat from the skin (Gjertz 1949, Whyte 1951). They have a very low heat

capacity and for that reason are cooled by the air immediately when removed from the skin surface. This could easily be observed from the galvanometer scale during the experiment. There was no anemization observed of the skin where the thermocouple was applied. The skin, however, was slightly anemized where the edges of the excavation of the pencilshaped holder was applied to the skin, but it only lasted about five seconds a minute on each finger. I never saw any measurable fall in temperature during the measurement even if the holder as a control was put against the skin for 15—20 seconds.

During some of the experiments the mouth and rectal temperatures were continuously measured. These measurements were made with a similar galvanometer and other holders. This instrument was not connected with the one used for determining the skin temperatures.

The rectal holder consists of a little rod-shaped capsule of thin metal. It is slightly wider at the base to be kept in place by m. sphincter ani. The measuring junction is adapted in the head of the capsule.

The mouth temperature was determined by a holder made of metal shaped as a small semi-ellipsoid with the thermocouple placed under the pole. During the experiments this ellipsoid was put under the tongue and the isolated cable departed from one corner of the mouth. After that the mouth was sealed with adhesive plaster to prevent the external air form interfering with the measurements.

4. The Room Temperature

Most earlier studies of human vasoconstriction and vasodilatation were made at varying room temperatures. Burton (1934), however, showed that the skin temperature among other factors depended on the temperature of the surrounding air. Since then many investigators have checked the room temperature at their investigations but not all of them have kept it at a constant level (for ref. see Bock 1952). Most authors used a temperature slightly above 20° C. Catchpole & Jepson (1954) advocate that a room temperature below 19° C is inappropriate. They could not induce vasodilatation with certainty by wrapping an electrical warming sheet around the body, despite the mouth temperature increasing at least 0.3° C. On the other hand, Wolff & Pochin (1949) showed that a room temperature of 20° C was enough to induce vasodilatation in most cases even after cooling the hands, and the finger temperature was augmented so that it almost attained body temperature. Heidelmann (1952) studied the temperature increase in the fingers after 5 minutes cooling in 15° C at a room temperature of 24° C. An increase within 20 minutes in every normal subject under 55 years was recorded.

Fetcher, Hall & Shaub (1949) deduced that there was no proportion between skin temperature and blood flow as measured plethysmographically other

than at a room temperature of —34° C and a skin temperature which was 55—66° C higher. At a room temperature of 7° C, however, they found a relative agreement between the methods, but hardly any at 21° C and 31° C. This statement was contradicted by Greenfield & Shepherd (1950) who did not consider finger-plethysmography as a reliable method at a skin temperature below 32° C.

Brattgård & al. (1951) used a room temperature of 15° C and no control subject failed to get dilatation of the vessels in the feet when their trunk and arms were immersed in a hot bath. In the experiments here described, I have chosen to work at a room temperature of 15° C as in our earlier investigation. If the room temperature is further decreased the room will be inconvenient to the subject as well as to the examiner. In some control experiments, however, I have worked at room temperatures of 18 and 20° C.

The air velocity in the room was below 1 m/sec. Even so slight air movement might influence the skin temperatures. Lower air temperatures, however, seem to diminish the influence of air movements on skin temperature between the ranges 15 and 30° C (Lotz & Wezler 1951). The air velocity of the room was kept about constant in all experiments.

5. The Humidity of the Room

Burton (1934) found skin temperature to be independent of the relative air humidity between 35 and 86 per cent. Winslow, Herrington & Gagge (1938) and Roth, Horton & Sheard (1940) analyzed the influence of air humidity on skin temperature measurements at room temperatures between 23 and 28° C. They considered a variation in relative humidity from 30 to 80 per cent to have less effect than a room temperature change of 0.6° C. Ratschow (1953) only advocates a relative humidity below 70 per cent. As I have worked at a lower temperature where too much humidity will make the air chilly, I have kept the relative humidity at a value of about 50 per cent.

6. The Cooling of the Hands

Most investigators who used the release of the vasoconstrictor tone in one or a couple of limbs through heating did not pay much attention to the initial temperatures of the limbs. None of the recent monographs on peripheral vascular disease mentions any skin temperature at which it is suitable to initiate increase in temperature through heating other parts of the body. (Ratschow 1953, Allen, Barker & Hines 1955, Samuels 1956, and Martin & al. 1956). Some investigators in this field have dealt with the problem. Morton and Scott (1931) considered it necessary to reduce the temperature of the digits preliminary before heating. Lindquist (1945) found that the most

rapid rise of temperature curves from the fingers was observed if the reflex vasodilatation was induced after cooling the hands in 15° C water at a room temperature of 14—16° C. Larsson (1946) considered that the borderline for the »normal vasodilatation level» in his material might be due to his using lower initial temperatures than others.

Many investigators had examined their subjects who had been sitting in the laboratory until the skin temperature was adapted to the surrounding temperature and had reached a steady state. As most investigators used a laboratory temperature of 18—24° C it was sometimes rather difficult to attain a steady state in the digital ends. It is more easy on other parts of the skin, which seems rather natural considering the importance of the arteriovenous anastomoses in the digital ends in the regulation of heat dissipation. Gahlen & Klüken (1953) measured the finger temperatures on several factory workers at a room temperature of 18° C and found two maxima in the curve on the distribution of temperatures, namely at 20° C and 31° C. Between these maxima, temperatures were most often oscillating. Landis & Gibbon (1933), Lindquist (1945), Larsson (1946) and Klüken (1955) also state that many persons may not be cooled only with air.

Vanggaard (1941) who used a closed box filled with air — in the walls of which there was circulating water at a temperature of 0.6—1° C — to cool the fingers, stated that the reaction of the finger vessels to cooling varied considerably. He found individuals who had a vasoconstriction induced, which was not relieved until vasodilatation was provoked from heating some other limb. Other individuals would show periods of vasoconstriction alternating with longer or shorter periods of vasodilatation (as shown in the fall or rise of temperature).

In the present investigation only 4 tests (16, 19, 22 and 24) were performed to cool merely with air. In none of these the cooling could reduce all the finger temperatures below 20° C. Two showed periods of increasing temperature up to 30° C on several fingers. Neither Redish, Sheckman & Steele (1952) could get stable temperatures on the fingers after two hours at 20° C in the room.

Thus, there is some evidence that air is no reliable medium of inducing vascular constriction. Water having much more heat conductive power and heat capacity is more reliable.

Brown & Page (1952) found that the temperature of the hands and the fingers equilibrated to a water bath, within 10 minutes, if the temperature of the bath lay anywhere between 5 and 35° C. Lewis (1930) observed »cold vasodilatation» (»hunting reactions») in the hands after immersion in cold water. This was never seen above 18° C, seldom between 18 and 15° C and with increasing frequency at lower temperatures in the hand bath. Greenfield & Shepherd (1950) re-investigated this reaction with a calorimeter and a plethys-

mograph and found that a bath temperature between 12 and 15° C gave a more slow, but also more pronounced inhibition of blood flow than lower temperatures. They did not notice any hunting reaction in a bath, warmer than 12° C. Wolff & Pochin (1949) reported that the more a finger was cooled, the greater the dilatation afterwards, even with a room temperature of 20° C as the only source of heat to provoke vasodilatation. Spealman (1945) observed a maximum vasoconstriction at 15° C in the hand-bath. A temperature of 15° C in a cooling bath has been used with success in similar investigations on feet (Brattgård & al. 1950).

In the present examinations there was hardly ever any sensation of pain in the hands at this cooling temperature, as was the case at lower temperatures (Schindler-Bauman 1945). The vasoconstriction induced, was constant for 18—50 minutes at a room temperature of 15° C without heating as I observed in 26 healthy controls.

In 13 other controls, under the same conditions the vasoconstriction was not constant. A varying increase in temperature was seen in some fingers, but only in three, was the increase so rapid and simultaneous that it resembled the temperature curves after heating the feet. The others showed a various appearance so that one or some fingers on each hand showed temperature increase, but not the other fingers. In the group of 13 controls the increase in temperature was often less than 1° C a minute or went stepwise for some minutes with intervals of more than one minute. Only one of these subjects reached the temperature of 32° C in all fingers. The others mostly showed falling temperatures after a period of rapid increase up to 20—29° C. The appearance of the temperature curves mostly resembled that seen in cases of various vascular disorders.

No »hunting reactions» were seen at the hand-bath temperatures of 15° C and no disadvantages found, disregarding the fact that some hyperthyreotic individuals got slight pains in their hands. I did not vary this bath temperature of 15° C.

No evidence has been brought forward in the literature indicating the time of cooling which induces a reliable vasoconstriction. Heidelmann (1952) used a cooling time of 5 minutes in 15° C water and measured the spontaneous dilatation induced by an air temperature of 21° C in the laboratory. A rise in temperature to the value before cooling was often completed in less than 9 minutes in his cases. The vasoconstriction did not appear to be reliable after that time. I preferred to begin with a cooling time of 10 minutes as recommended by Brown & Page (1952). If the temperature of the digits after that time was below 18° C a spontaneous increase in temperature seldom seemed to occur in a room temperature of 15° C. If the finger temperature was above this value there might be a definite vasoconstriction, but very often a spontaneous dilatation was seen despite the low room temperature.

Moreover, in 4 subjects (8, 22, 27, 28) the temperature of some fingers was not below 18° C after the cooling. These fingers showed increase in temperature soon after the heating had begun, but the increase was slow for several minutes. After that a phase of rapid increase in temperature followed but was not continuous in all fingers. In some it went stepwise with intervals of several minutes at the same temperature. Such curves were sometimes seen if the subject had a vascular disorder. In case the finger temperatures were above 18° C the cooling was continued for another period of ten minutes. There were only a few normal individuals who required more than ten minutes cooling. The need of prolonged cooling might indicate some degree of high BMR, which is dealt with in Chapter III.

7. The Heating of the Feet

To release vasoconstriction through indirect heating with a water bath most authors of text-books (Goetz 1956, Abramson 1956, Lynn 1956) recommend a bath temperature of 44—45° C. Only Allen, Barker & Hines (1955) are more moderate and advocate the temperature of 42—44° C. Brattgård & al. (1951) compared the temperature elevations on the toes on some individuals. They used constant room and cooling temperatures, but varying temperatures of the heating bath as mentioned before. It was found that the vessels of some individuals dilatated at a heating temperature of 38° C as well as 43° C. Others showed only an incomplete temperature rise in a bath of 40° C, but normal abrupt rise at 43° C.

In some experiments I controlled the relation between the temperature of the foot bath and the temperature curves of the fingers. If the bath temperature was below 41° C some individuals showed a prolonged period of latency. Moreover, there were intervals in the otherwise continuous rapid rise in temperature. Such intervals of a duration more than one minute were also seen in cases with vascular disorders. In one person (26) a normal temperature reaction with a comparatively long period of latency was achieved with a foot bath of 45° C. There was no rise at all when the foot bath had a temperature of 39° C. I have considered this phenomenon as a sign of the bath not being warm enough to induce inhibition of vasoconstrictor tone. Another subject (19) showed a slow increase in temperature in a couple of fingers and after that a decrease. Yet another subject (16) reacted with a normal increase in temperature to a foot-bath of 39° C.

I have also investigated the effect of a foot-bath that was too hot. In some individuals 45° C caused a distinct sensation of pain in the feet. Such pain could be followed by a tendency to vasoconstriction and lowered temperature in the fingers as seen in three individuals, (8, 10, 13), where a spontaneous increase in temperature had occurred after the cooling. The temperatures of

the fingers were rapidly rising when the subjects immersed their feet in a bath of 45° C. They felt pain and there was a prompt fall in the finger temperature for some minutes.

For reasons mentioned I consider the temperature limits used by Allen, Barker & Hines to be adequate. The higher temperatures advocated by the other authors of textbooks, may cause pain and vasoconstriction and, thus, disturb the measurements. Some of my earlier examinations were, however, performed with a bath temperature of 45° C. If there was no pain perceived the temperature had no influence on the results of the examination. Lower temperatures did not induce effective abolition of the vasoconstrictor tone induced. Practically all experiments in the present investigation were performed with a heating bath temperature of 43.5—44° C when the heating was begun. The temperature of the bath then slowly decreased, but in no case below 41.5° C after two hours of heating. This temperature in the bath ought to give a complete release of the vasoconstrictor tone in all normal individuals.

As all control subjects showed a rise in skin temperature when only the calves and feet were warmed, it seemed unnecessary to consider heating larger parts of the body.

8. The Position of the Subject

Investigators working with reflex vasodilatation place the examined persons in a position suitable to their mode of inducing release of vasoconstrictor tone. Goetz (1956), e. g., uses water containers to heat the legs, and places his subjects in a sitting position. He shows in a picture a subject sitting with straight legs. Abramson (1956) and Allen, Barker & Hines (1955) recommend a recumbent position and perform the heating with hot water bottles, electrical blankets or just hot boxes or cradles with bulbs.

It has been known for a long time that the position of a limb influences the skin temperature and blood flow in that portion (Grill 1937, Roth, Williams & Sheard 1938, Goetz 1950). In later years there has been accumulating evidence of the nature and magnitude of this influence. Goetz (1950) and Gaskell & Burton (1953) working with plethysmography noted that when the arm or leg was lowered there was a large decrease in the digital blood flow. Roddie (1955), however, found with calorimetry that the heat elimination on all levels below the reference point was slightly, but significantly greater than on the reference level, 4 cm above the sternal notch. The rate of heat elimination from fingers placed above this reference level was markedly diminished. Roddie & Shepherd (1956) found that elevating the legs of a recumbent subject caused a significant increase in the forearm blood flow, but no significant change in the hand blood flow. From these investigations and many others a conclusion can be drawn that the position of the subject must be

standardized in all investigations on circulation in arms and legs. No series of experiments should be compared to another without evaluating differences in the positions of the subjects.

9. Influence of Perspiration

Abramson (1956) writes in his monograph »The most obvious change elicited by body heating is sweating». This statement is no doubt true as regards the body in general, but may be questioned with respect to the fingers.

Perspiration might influence the heat elimination from the fingers, and, moreover, might disturb the thermoelectrical measurements.

In the control subjects and in the patients with diabetic and organic vascular disease no perspiration could be observed on the fingers during the experiment. Only in one case (S 16) of vasospastic disease were there signs of perspiration in the palms but not in the fingers.

The appearance of perspiration was controlled in 16 subjects. Immediately after the fingers had been carefully wiped dry after the cooling bath, they were stained with a rapidly drying solution of iodine (Iodine 1.5 g, Oil of ricin 10 g, Ethanol 99.6 per cent 90 g.). As soon as the iodine solution had dried the fingers were powdered with starch and the examination continued with foot bath and temperature measurements in the usual way. No signs of sweating from the fingers were seen.

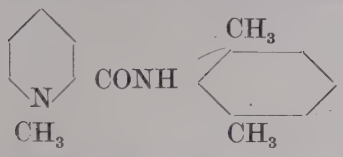
These observations are in accordance with the experiments of Burton & Taylor (1940) who consider the activity of the sweat glands in the hands to be independent of the activity of the cutaneous vessels. Also Vanggaard (1941) made similar observations. Kuno (1956) emphasizes that perspiration of hands and feet is elicited by nerve impulses and independent of increase in the body temperature.

The number of examinations on perspiration made in this work was too small to permit any definite conclusions about the sweating of the fingers during my experiments, but together with the observations of the authors cited, there is rather much evidence to indicate that perspiration had no influence on the present results.

10. The Ulnar Nerve Block

A method generally applied to relieve vasoconstrictor tone is conduction anaesthesia to peripheral nerves (Ratschow 1953). If the block is followed by complete peripheral anaesthesia the release of constrictor tone will appear in about the same area. The limit of the method is that only the little and perhaps the ring finger are dilated (Goetz 1956, Abramson 1956, Lynn 1956). The application of the nerve block was performed in order to establish if there

was any vasoconstrictor tone left in the fingers after the influence of the heating of the feet. The block was produced by an injection of 5 ml of 1 per cent carbocaine[1]) in the ulnar nerve channel at the elbow. The effect was tested with pinprick. Carbocaine is a new local anaesthetic with the formula



; HCl (Ekenstam & al. 1956). It was found to have the same anaesthetic effect without addition of adrenaline as lidocaine with adrenaline by Duhnér, Oljelund & Aaagesen (1957). Carbocaine proved to be a very good anaesthetic with a duration of anaesthesia for more than two hours. It was considered expecially suitable in the present study as the vasoconstrictor effect of adrenaline was avoided. No injurious effect was observed.

11. The Reactive Hyperaemia

The reactive hyperaemia, following a period of arrest in circulation, has been subjected to much discussion since the end of the 19th century (Cohnheim 1890, and Bier 1899). The cause of the hyperaemia has been ascribed to anoxaemia in the tissues (Krogh 1922), accumulation of histaminlike substances (Lewis 1927) or lactic acid (Rein 1941) and lack of pressure in the vessels during the occlusion (Folkow 1949, Patterson 1956). The cause of the phenomenon still remains obscure but histamine has been excluded as a probable cause (Emmelin & Emmelin 1947, Folkow, Haeger & Kahlson 1948 and Carlsten, Kahlson & Wicksell 1949). Bier already showed in animal experiments that reactive hyperaemia followed temporary arterial occlusion also if all neural connections between the peripheral vessels and higher nerve centres were broken. Müller (1937), however, was of the opinion that the nervous influence on reactive hyperaemia should not be totally disregarded.

The use of the reactive hyperaemia after temporary arterial occlusion in clinical diagnostics has been considered to involve risks of necrosis, especially in arteriosclerotic and hypertensive patients (Abramson 1956, Lynn 1956) and for that reason does not seem to be much used in Anglo-Saxon countries. According to Ratschow (1953) there is a difference in the origin of the flush, and the increase in temperature of the skin seen in reactive hyperaemia. The flush indicates a dilatation of the capillaries, which appears instantly after the release of the occlusion and remains unaltered for about 7 minutes. The increase in temperature indicates the dilatation of the arterioli and begins about 30 seconds later, but is slower. The increase in temperature will progress

[1]) Carbocaine is manufactured by AB Bofors Nobelkrut, Bofors.

for approximately three minutes. Ratschow also states that a delayed reaction, as regards the colour of the skin, is always connected with vascular disease, but vascular disease may be connected with normal reaction. As for delayed increase in temperature it is most often seen in vascular disease per se, but also in nephritis, sometimes in rheumatic disease and in heart insufficiency (Schneider 1940).

Ratschow advocates an occlusion time of 2 minutes or more. I have used an occlusion time of 5 minutes which according to Folkow, Thulesius & Grimby (1957) is followed by complete or almost complete relaxation of the vessels in the muscle. Perhaps some further relaxation could be induced through a prolonged arterial occlusion, but a prolonged occlusion was suspected to cause damage in tissues with already impaired circulation. No complications were observed.

The cuff was generally applied on the forearm immediately above the wrist. It was inflated as fast as possible by an ordinary rubber pump, and deflated in a couple of seconds by the valve of the pump. Such a slow deflation is not adequate when the reactive hyperaemia is measured in the forearm, where the increase in blood flow comes almost immediately. It is not believed to cause any disturbance in the present investigation as the temperature reaction is somewhat delayed.

12. **Roentgen Examinations**

Most roentgen examinations mentioned in the present paper were done as routine examinations. Some arteriographies of the arms were, however, performed especially for this investigation. They were reduced to include only patients with obscure vascular symptoms and some diabetics without vascular symptoms. The reduction was due to the hesitation found in the literature owing to the fear of complications when applying this method. Wagner (1956) e. g. advocates that vasospastic vascular syndromes are contraindications to arteriography, since this procedure aggravates existing spasm. Steiner (1956) suggests cautiousness considering the risk of arterial thromboses. He emphasizes, however, that arteriography is an important method in the study of Raynaud's disease and denies seeing any spasm caused by this operation. Ivins & Janes (1955) are of the same opinion. After this work was completed, Bartley & Wickbom (1957) have investigated the arteriographies of arms and legs performed at the Roentgen Department III of Sahlgrenska sjukhuset where most of the arteriographies, here described, were performed. They observed arterial spasm at the catheter-tip in 35 per cent of the examinations. Spasm was more frequent in narrow arteries, in young, and in female patients. Spasm occurred in all cases of Raynaud's disease.

In some diabetic patients the arteriographies were accompanied by intra-arterial injection of acetylcholine. The injections were performed in the brachial artery through plastic catheters (Seldinger 1953). Skin temperatures were followed during the examination. These examinations were carried out in an ordinary roentgen laboratory at a room temperature of about 21° C.

13. The Phases of the Temperature Curves

The temperature curves, studied in the present investigation, have been divided in some phases to facilitate the comparison of the individual curves between fingers and persons (Figure 1). These phases are defined as follows.

1. *Period before cooling.* This is when the patient is sitting in the laboratory ready to start the cool hand bath.

2. *Period of cooling.* This is when the subject has his hands in water of 15° C.

3. *Period of latency.* This is the time between the beginning of the hot bath and the commencement of the increase in temperature. This definition is taken from Gibbon & Landis (1932) who studied the increase in temperature on the toes, while the arms were tested.

In my investigations there are, however, some difficulties in defining both these limits. If a person is to put his arms in a bath, there is no difficulty to state the time of immersion, but if he is to place his legs in a bath, without making use of his hands, it takes some time. This time does seldom exceed 30 seconds, and never one minute, so that the beginning of the latency period may always be defined except for one minute. The consequence of this lack in accuracy will be discussed later on.

As has been pointed out by Brattgård & al. (1951) there is sometimes some difficulty to decide where the temperature curve from a digit shows an increase indicating a physiological response to the heating of the body. In that paper such an increase was considered to take place when the temperature of the toe was augmenting more than half a degree C each minute.

The increase in temperature of the fingers, as a reaction on heating the legs, is much more rapid. For that reason, I have decided to accept that the period of increase in temperature, i. e. in reality a period of rapid rise, begins when the temperature of the finger augments more than one degree per minute. The slow rise in temperature, which often, but not always, precedes this period of rapid rise is, thus, included in the period of latency.

4. *Period of rapid rise in temperature.* The beginning of this period is even now defined in Paragraph 3. As the finger temperature has attained a value of about 30° C the temperature curve has a tendency to become less vertical. The rapid rise is defined to end, when the increase in temperature is less than 1° C per minute.

5. *Increase in temperature.* This is the increase in temperature which occurs during the period of rapid rise in temperature.

There are authors, Vanggaard (1941) for instance, who have tried to use the temperature increase per minute as an indication of the dilatation of the finger vessels. In the present investigation there is no correlation found between these two terms. For that reason they have been calculated separately.

6. *End temperature.* The end temperature is the highest temperature measured on the finger after heating.

The periods of latency and rapid rise, the temperature increases and end temperatures are used as variables in the following statistical calculations (Chapter II).

B. Discussion of Methods

Through cooling of the fingers a vasoconstriction is generally induced. A vasodilatation may again be provoked through direct heating of the fingers. This proceeding, however, is difficult to associate with determinations on the circulatory variations. The information on the regulatory capacity of the vascular system will also be incomplete as the central regulation of vasoconstrictor tone is not tested. Some other way of relieving the vasoconstrictor tone is to be preferred. Reflex vasodilatation by heating is easy to perform and complete according to Arnott & Macfie (1948), does neither imply any punctures as regional anaesthesia nor any widespread loss of vasoconstrictor tone as the administration of tetraethylammonium- or hexamethonium-compounds (Abramson 1956). The only disadvantage is that the position of the patient must be varied during the experiment if not particular experimental conditions are purveyed (Goetz 1956).

The course of the reflex vasodilatation has usually been studied with plethysmography, calorimetry, pulse volume registrations or skin thermometry. There are objections to all these methods.

Digital plethysmography is not considered to give correct results when the fingers have been cooled. According to Greenfield & Shepherd (1950) the vasoconstriction induced in the finger by cooling makes the plethysmography erroneous. The readings from the cooled finger would not be valid until the temperature of 32° C was reached in the finger. It is still possible to follow the onset and course of vasodilatation after cooling with a finger plethysmograph, but the volume values obtained are perhaps no more valid for measuring the finger blood flow than skin thermometry.

The quantitative determination of the blood flow in the fingers through calorimetry depends on the knowledge of the temperature of the arterial blood flowing to the finger, and of the venous blood leaving the finger. Many

assumptions have been made on these temperatures. Most of them imply that the temperature of the blood, arriving at the finger, is the same as the oral or rectal temperature (Mendlowitz 1954). Bazett & al. (1948), however, showed that the temperature of the blood in the radial artery was much lower than the oral or rectal temperature. This low temperature was considered secondary to the »precooling» of the arterial blood from cool venous blood returning from the skin, especially the fingers. The calorimetry for that reason is useful only as giving the minimal value of the blood flow, i. e. the blood flow always must be greater than that calculated from the readings (Burton 1954). Eurman & Mendlowitz (1952) determined the arterial blood temperature simultaneously to the calorimetric readings. They found no true correlation between the oral temperature and the blood temperature in the radial artery, if the room-temperature was below 25° C. They concluded that the room-temperature should not be lower than 25° C and preferably exceed 29° C at calorimetric determination of finger blood flow. Calorimetry is, thus, not suited to be used in studying the blood flow during reflex dilatation.

If calorimetry is used to measure the blood flow during an increase in skin temperature from 15—35° C, there would always be a discrepancy between the skin- and the calorimeter-temperatures in some part of the temperature curve. That discrepancy probably would disturb the blood flow during some period of the vasodilatation. The same would certainly occur also with the metal measuring head of the »Strömungscalorimeter» by Hensel (1951).

For reasons mentioned, finger plethysmography and calorimetry cannot be relied upon to give really quantitative information about finger blood circulation during reflex vasodilatation.

Pulse-volume determinations are independent of the blood temperature of the subject and of the room temperature if it is constant (Burton & Taylor 1940). They only register the fluctuations of finger volume caused by the pulse wave. A rather good correspondence between blood flow and pulse volume records during reflex vasodilatation is demonstrated in fingers by Burton (1939), Burton & Taylor (1940) and Goetz (1956). The rise in finger temperature was delayed for some minutes as compared to the increases in volume. Goetz emphasized that the finger temperature could reach »normal vasodilatation level», (32° C) and yet the pulse volume be well below its minimum level for complete vasodilatation. I have not found any statement from Goetz about the readings of volume and temperature being obtained from the same finger. Some texts of the pictures (4.24, 4.25 e. g.), however, reveal that the temperatures are determined on another digit than that used for volume determinations. The other authors cited have used the same procedure. From the results of the present work it is evident that this mode of comparison is hazardous even

in healthy individuals and far more in patients with vascular disorders. Furthermore Goetz did not induce any vasoconstriction before heating of the feet and he kept the room temperature at about 20° C. For that reason his subjects could perhaps obtain finger temperatures of 32° C with less increase in blood flow than mine.

A vascular disorder of the arm is not always represented by abnormal reactions in all fingers. The circulatory disturbances of a generalized vascular disease are not as a rule equally distributed in the fingers. For reasons mentioned the determination of the circulation in all ten fingers should increase the validity of examination.

Most methods used in this field of investigation are too complicated to be arranged to study ten fingers at the same time. The work with digital plethysmography was performed on two fingers simultaneously (Goetz 1943, 1956, Abramson 1946, 1956, Burch 1942, 1947). Winsor (1953), however, reported the determination of blood flow to four fingers in rapid succession. Calorimetry is as a rule applied only to one finger (Mendlowitz 1954 e. g.). Photoelectric plethysmography (Hertzmann 1938, Dillon & Hertzmann 1939) and rheography (Kaindl 1953) may be applied at several points at the same time, but are technically complicated and difficult to calibrate. Hensel & Bender (1956) recently described an instrument to measure the power of heat convection of the skin, which they consider proportional to the blood content of the skin. The device seems to be applicable to several points simultaneously but has not yet been available for general use.

Skin temperature measurements have the advantage to other methods mentioned as being simple and applicable to all fingers almost simultaneously. The use of this method for estimating the blood flow in the skin has been criticized primarily because no numerical values of the blood flow are obtained (Cooper & al. 1949, Hensel 1952, 1956). From the discussion stated it is evident that the plethysmography, calorimetry and pulse volume determinations do not always give really quantitative values of the blood flow either. The objections against skin thermometry as giving less reliable information on the peripheral blood flow are thus not valid during reflex vasodilatation. Clearance of ^{24}Na from the skin during reflex dilatation has been observed well correlated in time and rate to the changes in skin temperature (Harris, Martin & Williams 1952).

The more the fingers and arms are cooled before provoking of vasodilatation the more reliable the finger temperature measurements. The precooling effect of the returning venous blood on the arterial blood coming to the arm will imply that constricted peripheral vessels with a small blood flow only receive blood with a considerably lower temperature than the deep body temperature. To permit warm blood to pass the peripheral vessels to such an extent as to be manifested by an increase in temperature, a more complete

vasodilatation is necessary when the »precooling» is pronounced than when it is slight. The suitable temperatures for the experiments have been discussed.

Conclusions: Reflex (indirect) vasodilatation should be an appropriate method in the clinical study of the circulation of the fingers resembling the physiological variations of the finger blood flow. Temperature measurements of the finger skin are as reliable as other methods in estimating the blood flow during reflex vasodilatation. Temperature measurements can be obtained from all fingers almost simultaneously, which increases the diagnostic value of the examination.

Gibbon & Landis (1932) suggested that the return of heated blood from one extremity released vasodilatation in the others. Pickering (1932) considered an increase in body temperature to stimulate the thermosensitive centres in the hypothalamus initiating vasodilatation. He estimated the rise of body temperature required to stimulate the hypothalamic centres to only 0.01—0.04° C. Fatherree & Allen (1938) and Goetz & Ames (1949) have performed extensive studies demonstrating that reflex dilatation in the hands depends on the return of blood from the legs and the integrity of the nervous supply of the arms. Goetz & Ames pointed out that the circulation of the legs must be good, considering the steepness of the rise in blood temperature to initiate the reflex dilatation of the hands rather than the actual body temperature. The blood temperature most certainly is important for eliciting the vasodilatation response. Folkow, Ström & Uvnäs (1949) and Ström (1950) have shown that local heating of the anterior hypothalamus causes a cutaneous vasodilatation in the limbs of the cat. The heated blood returning from the legs probably accomplish the heating of hypothalamus in reflex dilatation.

Kerslake & Cooper (1950) revealed that vasodilatation of the hand could be elicited within 15 seconds after heating the skin of the trunk. They also got vasodilatation in the hands on heating the legs when the legs were excluded from the circulation with pressure cuffs round the thighs inflated to 200 mm Hg. This evidence is somewhat confusing. The vasodilatation in these cases, however, was elicited with a very short period of latency, seldom seen at the reflex vasodilatation described in this work. As believed by the authors a purely nervous reflex most probably was working in the dilatation observed by Kerslake & Cooper. This reflex mechanism probably has no connection with the reflex dilatation described in the present work.

In the present work the patency of the circulation in the legs was tested in all subjects and patients by pulse palpation and oscillometric readings. As the circulation of the terminal (arteriolar, capillary, and venular) vessels could be impaired in the generalized diabetic angiopathy, and thus disturb

the results of the examinations, the correct return of warm blood from the legs ought to be tested in some way. In some patients oral and rectal temperatures were observed continuously. As is evident from Table V no reliable increase in temperature could be observed even when the finger dilatation was completed. Neither any increase in these temperatures was regularly observed before the rapid rise in temperature commenced. The observation of oral and rectal temperatures therefore was not considered to supply any valuable information and was discarded from the rest of the experiments, especially as these measurements were irritating for the patients. The problem of the circulation of the legs will be further dealt with in Chapter V.

CHAPTER II

THE CONTROL MATERIAL

A. Introduction

The control material originally consisted of 81 persons: 41 males and 40 females. All of these had some connection with the hospital. The females were superintendents, trained nurses, assistants, and probationers, the males were doctors, medical students and warders. I am aware that the sampling is somewhat limited, but it is hardly possible for other quite healthy persons to attend examinations at the time when patients are generally examined. I have not tried the possibility, often used, to employ hospitalized patients, whose diseases have no obvious connection with the vascular system. In my opinion most diseases requiring hospital care may have some influence on the vascular system.

To ensure that the control subjects were healthy at the time of examination a two-stage procedure was used. At the first temperature examination a short history was taken and a general inspection performed. Two questions were always put to the subject. 1. »Are you feeling completely healthy?» and 2. »Have you ever suffered from cold and pale hands or feet?» If the first question was answered in the negative the examination was cancelled. If the second question was answered in the affirmative the subject was examined, and sometimes referred to the material of vascular disorders.

Three months to a year after this occurrence, in a couple of cases even more than two years, a thorough examination of the subject was done. This examination consisted of a more comprehensive history, a general physical examination of the subject including heart, lungs, abdomen, and tendon, pupillar and plantar reflexes. Furthermore, a more specialized examination of the circulation was performed including inspection of the hands and feet, palpation of the pulses on wrists and ankles and an oscillometry on these locations. The urine was tested for protein and sugar. Radiological and ECG-examinations were generally not performed. Most of the control persons had been subjected to an X-ray of the chest less than two years before the present examination. From the initial 81 persons two were excluded because they had had cold, pale fingers. Another 11 subjects were excluded for various reasons, previous cold injury to the fingers four, active pulmonary tuberculosis,

bronchiectasis, marked heart insufficiency, peptic ulcer, severe injury to one wrist, sensitivity to tobacco, and previous attack of encephalitis (however not verified) one of each.

After the exclusion the material consisted of 68 persons: 35 males and 33 females, without symptoms and signs of disease.

The material was divided according to age in three classes. The limits of classification were under 30, 31—45 and 46—60 years of age.

The group of age under 30 years consisted of 37 individuals between 19 and 28 years. There were 14 females (19—27 years, mean 22.5) and 23 males (22—28 years, mean 24.3).

The group of 31—45 years included 19 subjects from 31—44 years of age, 12 females (31—44, mean 37.4) and 7 males (31—41, mean 37.3).

The group of more than 46 years contained 12 subjects between 45 and 58 years, 7 females (47—56, mean 51.3) and 5 males (45—58, mean 52.4).

There were comparatively many young people included in the material and comparatively many males in the youngest group, females in the oldest.

No statistically significant differences in the material according to age or sex were found, but for the tendency of older individuals, to show a prolonged period of latency in one hand, as compared to the other (cf Chapter II B). These statistical differences between the fingers and between the means of the hands most probably should be and also were disregarded. The uneven age and sex distribution therefore was not considered to diminish the value of the material as a control group.

In physiological investigations on the function of the peripheral vascular system there is a general demand that the observations ought to be done under similar conditions. This is also desirable in clinical work, but often difficult to attain. In many standard clinical examinations such as BMR, blood chemistry, and blood morphology the standard values were calculated on examinations made on subjects during standard stipulations such as body rest, empty stomach, etc. Every physician knows that these standards cannot always be kept up, as the patient is not available at the suitable time, is disturbed in some way or has eaten.

The aim of the present investigation on the control material was to standardize the method of reflex vasodilatation in the hands, studied by skin temperature measurements, so that it might be used in practical clinical routine. I therefore only standardized the surrounding conditions such as the room, the baths and the order of the examination. At the first examination the subjects were permitted to come when it was suitable for them. The hour of the investigation varied from 8 a. m.—4 p. m. hours. Some subjects had eaten and others not. Of those who were smokers some had just smoked and some not before the examination. To control the most obvious deviations of time and personal habits, some examinations

were performed in the morning on a fasting stomach, and compared with examinations on the same persons after lunch. A group of female controls were examined in the pre- and postmenstrual periods. Some duplicate experiments during as similar conditions as possible were also performed. Smokers were compared with non-smokers and those examined in summer with those examined in winter.

All control subjects were connected with hospitals and thus accustomed to all sorts of examinations. For that reason the influence of psychical reactions on the examination results could be neglected.

B. Results

The results have been treated statistically.[1]) To establish the limits of the curve values that are compatible with a normal finger circulation the variables defined in Chapter I D (i. e. period of latency, period of rapid rise in temperature, temperature increase and end temperature) have been determined for each finger. From every subject there are, thus, 10 determinations on each variable and four variables determined on each finger, as a whole 40 determinated factors which are calculated. As there was no correlation between these 4 variables they were calculated separately. In this calculation only the first examination without technical fault on every subject was included. The calculation has been variance analysis in the same manner as Brattgård & al. (1951).

1. Age and Sex Variations

At first the influence on the results caused by age and sex variations was calculated (Table I). There was no significant difference between the male and female groups compared ($P > 0.2$ in all variables).

For that reason it was considered permissible to add the male and female groups before comparing the age groups. There was no correlation either between the age and the variables ($P > 0.2$ respectively)

The age and sex variations of the variables calculated, thus, were not statistically significant. The control material could therefore be regarded as consisting of individuals similar in character and be treated as a homogeneous group (Table I).

The age and sex variations of the subjects could also be disregarded with consideration to the variations induced by the time of the year, menstruation period, time of the day, and tobacco habits.

[1]) The statistics of this work has been designed and looked through by professor C.-E. Quensel at the University of Lund.

It could be suspected that any of the fingers might deviate from the others e. g. the right thumb being more exercised than the other fingers or the left ring finger often carrying rings. No such systematical deviation was observed (Table II).

2. Control Determinations on the Same Subject

The individual variation was determined. Thirteen control persons were subjected to examinations at approximately the same time of the year, the same time of the day and the same phase of the menstrual period. The differences between the determinations were determined so that the values from one examination were subtracted from the values of the other. The standard deviations (S. D.) of the differences were calculated and the results are seen in Table III. There was a considerable variation concerning all the variables except the end temperatures. As regards the difference between the first and second examination both increase and decrease were observed in all variables. Consequently there was no effect of the experience.

3. Influence of Time of the Day and State of Digestion

Aschoff (1955) stated that the temperatures of the extremities participated in the twenty-four hours variation of body-temperature but was inverse to the oral and rectal temperatures.

Seven subjects were examined on empty stomach in the morning, and another day after lunch. The other conditions were approximately the same. The differences between the two examinations were determined so that the values of the morning examination were subtracted from those determined after lunch. The standard deviations of these differences are seen in Table III. The morning determinations give slightly smaller values, but this difference is insignificant as compared to the individual variations described in Paragraph 2.

4. Influence of the Menstrual Period

Heidelmann (1953) pointed out that the tone of the arterioles in the digital ends was higher in the follicle hormone phase than in the corpus luteum hormone phase. To find out if there was any similar influence on the present method, seven females were examined within 12 days before the onset of the menstruation and in the first week afterwards. The postmenstrual values were subtracted from the premenstrual ones and the differences calculated. The standard deviations of these differences are seen in Table III. It is obvious that there are no significant differences between these two examinations (as compared to the individual variation).

5. Influence of the Room Temperature

To keep a constant room temperature of 15° C is the most difficult, and above all, most expensive stipulation to fulfil in the present manner of investigation. To determine the influence of various room temperatures some experiments were performed at 22°, 20° and 18° C.

Three of the control subjects had their hands cooled in the usual manner at a room temperature of 22° C. In no case the finger tips could be cooled to 15° C in 10 minutes. The temperature in some of these cooled fingers increased spontaneously immediately after the cooling was ended, and the temperature in all of them increased in a couple of minutes without heating the feet. One of these subjects had her fingers cooled in water of 10° C at a room temperature of 22° C. Now the finger temperatures remained at about 14° C for some minutes but within 6 minutes an increase was observed in all fingers without heating.

Nine subjects had their hands cooled in water of 15° C at a room temperature of 20° C. The finger tips of one subject could not be cooled effectively. A spontaneous rise in temperature was noticed as soon as his hands had left the cool water. The others showed temperature of the fingers about 15—17° C as generally seen, and their feet were heated as usual. The values of period of latency, period of rapid rise in temperature, increase in temperature and end temperature at 20° C were subtracted from the corresponding values of the same individual obtained at a room temperature of 15° C. The calculations were performed as in Paragraph 3. (Table III).

The same experiment was performed on 10 subjects at a room temperature of 18° C. The differences were determined and calculated in the same way as mentioned above (Table III). In this group the cooling was always effective and no spontaneous rise in temperature was seen.

The table shows that there is no significant difference between the measurements at a room temperature of 18° or 20° C and the values obtained at the usual room temperature of 15° C.

The *conclusions* of the experiments described in this paragraph are:

1. At 22° C in the room the fingers show too great a tendency of spontaneous rise in temperature even if a lower cooling temperature is used.

2. If the temperature of the room is between 15° and 20° C, the temperature curves of the fingers on heating the feet will have the same configurations, if the cooling is effective. It has earlier been pointed out that the humidity of the surrounding air seems to be almost insignificant in skin temperature measurements. As it is possible to vary the room temperature in rather wide limits, experiments of this type should be possible to perform also in a room without air conditioning.

6. Influence of the Time of the Year

Bárány (1955) tested the influence of the time of the year on heat dissipation during body heating and regional anesthesia of 83 healthy males between 15 and 30 years of age. He found no significant difference between his values from the period of February—June as compared to the whole year during body heating. A marked influence of the time of the year was observed, however, if regional anaesthesia was used to relieve vasoconstrictor tone. I tested my corresponding group of 23 males between 15 and 29 years of age in a similar manner. As I considered my material too small to be divided in monthly groups, I only compared a summer group of 14 individuals examined between May 1, and October 31, 1954, and a winter group of 9, examined between November 1 and April 30, 1955. There was no connection between the season of the year and the variables ($P > 0.2$ in all). When the dispersion of values of the variables was studied on the whole material in relation to the mean value, it was observed that the number of values above and below the mean was about equal in the summer and winter groups. For that reason there is no evidence indicating a seasonal influence on the results of the present investigation.

7. Influence of Occupation

There were only two outdoor-workers (54, 68) in the control group. They did not show any deviations from the material in general. Bárány (1955) found a more efficient heat dissipation in outdoor- than in indoor-workers among diabetic patients. The difference was not statistically significant. His finding was in accordance with the results of Brown & Page (1952) on the hand blood flow in the Eskimo. In the present investigation outdoor-workers would thus probably show shorter periods of latency or rapid rise in temperature, and higher values of increase in temperature or end temperature, than indoor-workers. For that reason the values of the outdoor-workers would be well within the limits of the normal values calculated from the present material. These limits would possibly have been closer if the number of outdoor-workers had been greater in the material.

8. Influence of Smoking

The smokers and non-smokers were almost evenly distributed in the material. There were 35 smokers and 33 non-smokers. Only in the oldest groups all the males smoked and there was only one female who smoked. For the calculation of the differences between these groups the same examination was used that was included in the calculation of the variance of the whole material. There was no significant connection between the habit of smoking and the variables ($P > 0.2$ in all).

Two individuals, however, showed that smoking is not without influence on the experiments in this investigation. A male of the youngest group (51) who was a heavy smoker, showed at one examination, an increased period of latency and a pathologically small increase in temperature on the right thumb. He had just before the examination smoked three Virginia cigarrettes in succession. Another control experiment, under the same conditions, showed the same influence on the same finger. The experiment included in the calculation on the control group showed no divergence from the general appearance in the group. He had only smoked half a cigarrette before the examination last mentioned.

Another young male smoker, who had not smoked immediately before the examination, showed abnormally long periods of latency of 9 respectively 10 fingers on two examinations. On one of these the end temperatures did not reach more than 28° C in the thumbs. As he had suffered from a severe nephritis at the age of 7, and had recently had precordial pains he was excluded from the control group although he did not show any signs of disease at physical examination, or on ECG. He ceased smoking because of the precordial pains. The pains disappeared and about three months later the result on examination was almost normal with only one finger showing a pause in the rise of temperature.

Two other experiments were performed to determine the influence of smoking. One of the young males had stopped smoking more than three months ago. He volunteered to smoke three cigarrettes in succession immediately before the examination. He felt a slight dizziness, but the results of the temperature measurements were not influenced.

The other experiment was done on a male in the middle age group who had smoked 10—15 cigarrettes a day regularly for about 20 years. One examination was done in the usual way. The feet were after that given a short cool bath to reduce the vascular dilatation of the legs, and he was left to rest for an hour. During the last 10 minutes of that hour, three cigarrettes were consumed with deep inhalations. Another examination was performed with approximately the same result as the first.

From these experiments it is concluded that smoking ordinarily does not influence the results of the examination. Some individuals are perhaps more sensitive to the action of tobacco than others. For that reason smoking should not be permitted immediately before an examination.

C. General Discussion of Statistical Results

The results of the investigation on the control group were intended as a basis for forming an estimate of the results obtained by the investigation of individuals with vascular disorders. Before this application it must be

analysed if the control group was approximately representative of the healthy population.

To permit a control of the group of healthy individuals the total of 2 respectively $3 \times$ S. D. was added to the mean values. Only the values of the total material (stated in the large squares of Table I) were treated in this manner, no signs indicating that sex or age variations interfered significantly with the results.

The one limit of the 4 variables was always permanent. The period of latency and the period of rapid rise in temperature could not be less than 1 minute. As the temperatures of the fingers were about 15° C after cooling, and after heating could not exceed the body temperature there were also natural limits for the two temperature variables. For that reason only the maximal limits of the time variables are stated. As the determination of the periods was done only in whole minutes, the time values were rounded off upwards and given in full minutes. For the temperatures only the minimal limits are listed and as they were measured in tenths of degrees centigrade they are rounded off to the nearest half degree. The results are listed in Table IV.

When the variables used were defined, it was stated that there existed some difficulty to determine the beginning of the period of latency exactly. As the error could amount to one minute, another minute was added to the values for the periods of latency.

Classification of the Deviations from the Normal

The abnormal courses of temperature curves which can appear (Figure 2) were classified as follows:

I. *With a period of rapid increase in temperature.*

a) The continuous increase in temperature of more than 1° C/min. during the period of increase, ceased for a minute to continue as usual. The variables increase in temperature and period of rapid rise still attained normal values.

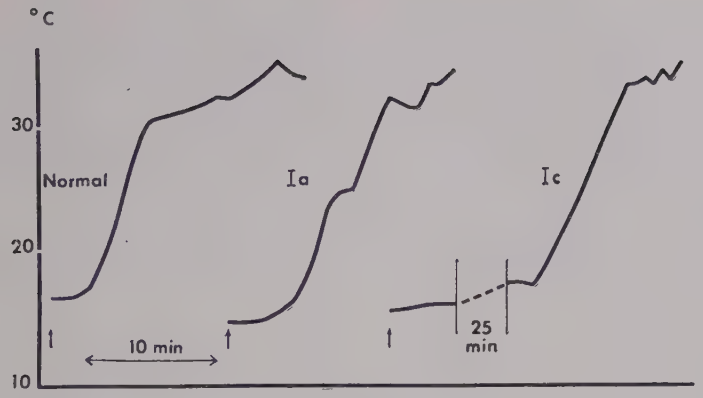
b) Some of the 4 determined variables were normal when measured in a single finger, but deviated when compared with the mean of the hand, or the mean of a hand was normal when measured within the hand, but deviated if compared with the other hand.

c) The period of latency was too long.

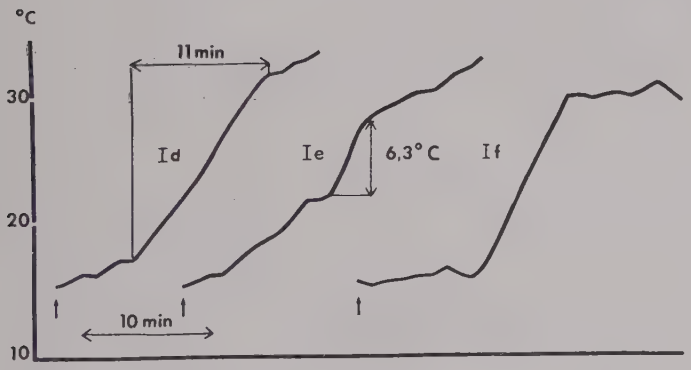
d) The period of rapid rise in temperature was too long.

e) The increase in temperature was too small.

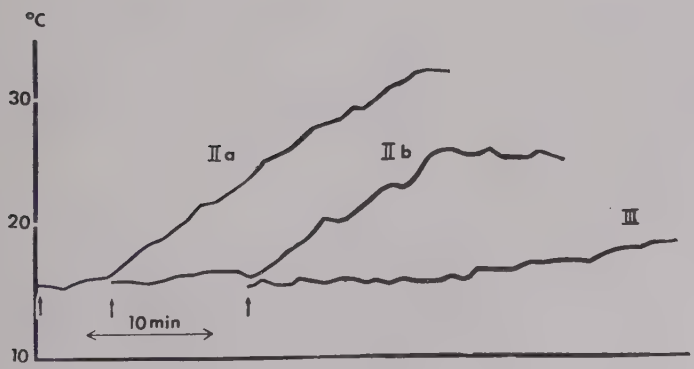
f) The end temperature was too low.



a.



b.



c.

Figure 2. *Examples of the Normal Course of a Temperature Curve and the Various Deviation from this Course described in Text.* The arrows denote the commencement of heating.

II. *Without period of rapid increase in temperature.*

No rapid increase in temperature was defined to occur when the greatest increase in temperature more rapid than 1° C/min. did not exceed 4° C.

a) The end temperature reached, lies within the limits of 3 × S. D.

b) The end temperature did not reach this limit.

III. *Without increase in temperature after the cooling.*[1])

No increase in temperature was considered to occur if the finger temperatures did not exceed 19° C at the end of the experiment after 35 minutes heating or more.

In the control group the deviations to be found were only of the types I a)—I e). For that reason all other deviations were considered more important for determining a finger as pathological. The deviations of the control group were always slight even if the repeated examinations, not included in the statistical evaluation, were considered. Most of the deviations were slight intervals of one minute in the continuous increase of temperature, or slight statistical deviations from the mean values of the hand of otherwise normal individual values. Neither the deviation of the period of rapid rise, nor of the increase in temperature were outside the limit 3 × S. D. The deviation of end temperature was never outside the limit 2 × S. D. There was only one finger deviating outside 3 × S. D. as regards the period of latency.

If a dispersion of 3 × S. D. was tolerated there were eight fingers deviating each having one cause of deviation. With 2720 possibilities to deviate the ratio is 1/340. The corresponding ratio is 1/57 if only 2 × S. D. is tolerated. Dahlberg (1940) states that by using the probability equation it is possible to calculate that in a normal distribution 2 × S. D. is exceeded once out of 22, and 3 × S. D. once out of 370.

If the fingers are regarded as independent variables there is a fairly good agreement between the exceeding deviations expected and those recorded. The eight fingers (3×S. D.) were, however, distributed on three subjects and the 48 fingers (2×S. D.) on ten subjects respectively. A number of individuals diverging to such an extent are obviously not desirable in a group representing a normal state.

A more thorough analysis of the deviations was therefore performed to establish if any of these could be tolerated.

1. The slight intervals in the increase of temperature of one minute with otherwise normal course of the temperature curve (I a) could not with certainty be regarded as the result of a pathological event. For that reason these deviations were tolerated as normal.

[1]) The Roman numerals followed by the small letters are placed in brackets in the text to denote the art of deviation from the normal.

2. On comparison between fingers a certain dispersion of the variables within the normal hands was observed. To select the most fluctuating variable, the period of latency had a dispersion of 1.41 minutes (S. D.). An arbitrarily selected finger has a probability of 3 promille to deviate from the mean of the hand more than $3 \times 1.41 = 4.23$ minutes. The most extreme finger, however, should have a probability of 3 per cent to deviate from the mean of the hand with more than this time. The statistical deviations from the mean values of the hands and between the hands for that reason are not so reliable as the maximum and minimum values of the variables for the single fingers. For reasons mentioned these statistical deviations were considered as normal, the finger variable values being normal when calculated separately.

When these limits of tolerance were added to the statistical limits there remained only one finger outside the limits of $3 \times$ S. D. and 3 subjects with fingers outside the limits of $2 \times$ S. D.

Such a dispersion outside the limits is well in accordance with the probability equation when the control subjects are calculated as individuals.

D. General Discussion on the Results of Examination

1. The Signification of the Period of Latency

Most investigators using reflex vasodilatation in clinical diagnostics have restricted their interest in the temperature curves to the periods of latency, and the minimal temperatures that should be attained by the digits during the examination (i. e. the end temperature in the present work).

Gibbon & Landis (1932) introduced the conception period of latency as the time between the beginning of heating and the onset of increase in temperature, and found that this did not exceed 15 minutes in six patients. Pickering & Hess (1933) found the same maximal value of the latency period for the fingers but, for the feet, two hours of heating could pass without signs of increase in temperature. The difference in response between the upper and lower extremity was attributed to a difference in the ability to abolish vasoconstrictor tone.

Uprus, Gaylor & Carmichael (1936) considered that a prolonged period of latency could not be accepted as an indicator of disturbance in the nervous regulatory mechanism of the blood vessels in subjects showing a slow increase of blood temperature. They believed the blood temperature in the central parts of the body to be equal to the rectal temperature. Burton & Edholm (1955), however, summarized all previous work on body temperature with the conclusion »that no one site or one reading of the deep core temperature can

give a figure which can be used to follow changes in the average temperature of the deep core».

In the present work there was no distinct increase in rectal or oral temperature found within the temperature examinations on control subjects. For that reason the increase in temperature of the fingers, following heating of the feet, is not considered to be dependent on an increase in body temperature (Chapter I).

The result of the publication of Uprus, Gaylor & Carmichael seems to have been that the periods of latency were considered irrelevant. In the recent monographs on peripheral vascular disease (Ratschow 1953, Allen & al. 1955, Samuels & al. 1956, Lynn & al. 1956 and Abramson 1956) the conception of period of latency is not even mentioned.

Brattgård & al. (1951), however, demonstrated that the period of latency was varying below the limit of 24 minutes if the conditions of the temperature examination were standardized. The corresponding upper limit in the present investigation was shown to be 30 minutes which may seem confusing as compared to the results of Pickering & Hess (1933). According to Fløystrup & Skouby (1950) the latency periods were related to the area of skin which was heated. Brattgård & al., however, heated the trunk and the arms, and in the present investigation only the calves and feet were heated. Thus the results of Brattgård & al. and the present investigation are in accordance with the findings of Fløystrup & Skouby as well as the conception that the vasoconstrictor tone is easier to release in the arms than in the legs (Roth, Horton and Sheard 1939/40). For further discussion see Chapter V.

2. The Signification of the Period of Rapid Rise in Temperature

Brattgård & al. (1951) introduced the definitions period of rise in temperature, and the increase in temperature during that period. During that period the increase in temperature was defined to be more than 0.5° C a minute. In the present investigation on fingers, however, the rise in temperature was much more rapid. The same was found by Vanggaard (1941), and for that reason the demands on the rise in temperature were increased to 1° C a minute. To mark the difference in demands the word rapid was included in the term. It should be emphasized that a period of rapid increase must be found on every normal finger measured according to the present method.

3. The Signification of the End Temperature

Most authors who give figures for the minimum temperature of the digital ends after reflex dilatation, compatible with a healthy circulation, make reservations as to the lack of systematical experiments on large series behind

these figures. The minimum temperature that must be attained is stated as 30° C by Abramson (1956) and Goetz (1956) and as 35° C by Lynn (1956) at a room temperature of 20° C. »The normal vasodilatation level» of Morton & Scott (1930), cited by White, Smithwick & Simeone (1952), is a skin temperature of 33.5° C after reflex vasodilatation (room temperature 20° C). There is thus some discrepancy of what is tolerated as normal.

Brattgård & al. found the temperatures of the toes to be 33.47 ± 1.12° C on 20 young students after heating the body during otherwise the same conditions as in the present investigation. For practical use the lower limit tolerated was 30° C with a tolerance of 3 × S. D. and 31° C with 2 × S. D. In the present investigation the mean of the fingers is about 1° C higher, and the dispersion less marked and therefore the lower limit of the end temperature is 32° and 32.5° C respectively on the fingers.

Summary

Sixtytwo healthy subjects were examined with the method of measuring the vasodilatation in the fingers as described in Chapter I. The results are not significantly influenced by the sex or age of the subject. No influence is either seen by the time of the day or year or the state of digestion. The habit of smoking may disturb the results but as a rule does not. The material is considered to be representative for the healthy population. The results are discussed in relation to similar investigations by other authors.

CHAPTER III

PATIENTS WITH DISORDERS OF THE THYROID FUNCTION

A. Introduction

Blood flow in the skin of the body measured in ml/m² body surface is increased in hyperthyroidism as observed by Steward & Evans (1940). The blood flow was diminished if the patient was treated with iodine and further diminished if subtotal thyroidectomy was performed. They found a linear correlation between the basal metabolic rate (BMR) and peripheral blood flow. This connection was valid for the skin of the trunk but was not extended to the surface temperatures of the extremities. The lack of correlation was perhaps due to the varying temperature of the room, 23—27° C, during their experiments.

Sheard & Williams (1940) working at a room temperature of 25° C and relative air humidity of 40 per cent, established that in healthy persons there was a linear correlation between the skin temperature of the big toe and the BMR. The deviations were, however, rather large. There was no connection between the toe temperature and age or sex of the subjects, seasons or other similar influences. The lower parts of the legs and the feet seemed to be of importance for regulating the heat dissipation of the body at an environmental temperature of 23—28° C, which was considered comfortable for a naked subject.

Eichna & Wilkins (1941) performed plethysmographical investigations on the forearm and hand on 5 hyperthyrotic individuals, one hypothyrotic and one with low BMR in connection with muscular dystrophy. The blood flow was found greater in hyperthyrotic persons than in healthy controls both at rest and after induction of reactive hyperaemia. The flow was reduced with decreasing BMR. The blood flow was diminished in hypothyrotic individuals but showed an increase during thyroid gland therapy.

The results of Stewart & Evans were controlled by Roth & Sheard (1950) with similar results.

Hyperthyrosis has not been considered to cause any peripheral vascular disease. *Hypothyrosis* on the contrary seems to provoke arteriosclerosis

(Allen, Barker & Hines 1955), perhaps due to the increase in the blood cholesterol, generally observed in connection with that disorder (Kramer & Perilstein 1956).

To estimate the influence of thyroid activity on the skin termperature measurements in the present investigation, patients with hyper- and hypothyrosis were examined before and after therapy.

B. Hyperthyrosis

The material included 17 patients (Table VI), who all suffered from hyperthyrotic disease, which demanded therapy.[1]) All these patients showed normal values of oscillometric readings at the wrists and their wrist pulses were also normal. None had symptoms or signs of insufficiency of the heart. The determinations of BMR were performed as routine tests and the method was not specially controlled for these examinations.

In 9 examinations on 7 patients (T 5, 7, 8, 10, 11, 13, 17) *it was impossible to cool the hands to the desired temperature of about* 15° *C in spite of repeated cooling periods of* 10 *minutes*. Finger temperatures between 19° and 27° C were obtained, mostly about 25° C. This phenomenon never occurred in the rest of the control and patient materials. Some of the patients with hyperthyrosis were the only individuals who felt real pain in the hands on immersion in water of 15° C. It may be assumed that this phenomenon was due to the great difference in temperature between the hands and the water, but the finger temperature of these patients in the period before cooling was generally not above that recorded on controls. The cause of the pain remains obscure. Of these 7 patients 3 were re-examined after subtotal thyroidectomy (T 7, 8, 13) and 2 after ^{131}I-therapy (T 11 and 17). These examinations were performed 1—6 months after therapy. In all patients where a reduction of the value of BMR had been obtained the values of the two variables of time and the two of temperature were well within the control limits of 3 × S. D. Only in one case (T 8) values outside the limits 2 × S. D. were seen, but that examination was not quite successful as the patient had a short attack of cramp in one of her legs just as she was getting into the warm bath. She sometimes got cramp at unaccustomed movements.

The other 10 patients all demonstrated comparatively short periods of latency as compared to the mean of the control material. The other variables, however, did not show any deviations from the control values. At the repeated examinations after subtotal thyroidectomy in three of these cases (T 4, 9 and 16), two cases (T 4 and 16) showed a BMR of +9 per cent and zero respectively and now had rather prolonged periods of latency compared to the values

[1]) Most of this material was supplied by the Surgical Clinic I, Sahlgrenska sjukhuset.

recorded before surgery. The mean prolongation was well above 3 × S. D. as calculated on two similar investigations on the same individual (Table III) and is thus statistically significant. The third of these cases showed a BMR of −10 per cent. The mean period of latency in the hands was prolonged from 0.6 to 24.3 minutes but there were also deviations of the increases in temperature outside the limits of 3 × S. D. in both thumbs. Her temperature records were now comparable to those seen in hypothyrosis.

C. Hypothyrosis

This material included 10 patients with a low BMR (Table VII). All of them had normal oscillometric readings and normal pulses at the wrists and no complaints of their fingers. Two of the patients (M. 4, 13) had normal temperature curves in spite of low values of BMR, −33 and −34 per cent respectively. The clinical symptoms of myxoedema of these patients were slight so that their diagnosis had been overlooked for some time in spite of repeated medical examinations. The duration of these two cases was 2 years and 3 months respectively.

One of the patients (M 8) with a history of nine years after subtotal thyroidectomy showed one finger on each hand with individual values of the period of latency well within normal limits, but deviating from the means of the hands. Otherwise all values were normal.

The remaining 7 patients showed various deviations from the results in the control group. The most remarkable observations were:

1. Failure to induce increase in temperature (III) within an hour (M 2, 3).
2. Slow increase in temperature, without end temperatures above 32° C (II b) in cases M 3, 7 and 9 and with end temperatures above 32° C (II a) in cases M 1, 2 and 6.
3. Periods of latency prolonged (I c) in cases M 1 and 12.

Thyroidotherapy was introduced in all cases. In two there was no success because therapy provoked severe precordial pain independent of the dosage (M 1, 2). ECG showed signs of coronary disease in both patients. They had suffered from their disease for 15—20 years according to the history. The temperature examinations demonstrated a slower increase on repeated examinations.

In 3 patients (M 3, 6, 9) the thyroidotherapy clinically corrected the myxoedema. Control values of BMR, however, were not obtained from more than one of these patients. Almost normal values for all variables were achieved in these cases on re-examination. In case M 5 and M 7 the periods of rapid rise were prolonged in one finger of each (I d). Case M 9 failed to reach end temperatures above 32° C in the fingers of the right hand, the finger tempera-

tures not exceeding 31.4—31.6° C. In this case reactive hyperaemia was applied but no further increase in temperature was obtained.

Case M 7 had neglected therapy at times. Her temperature examination showed normal results on all fingers at the first examination, but abnormal on some fingers at the second.

The other 4 cases could not be re-examined.

D. Discussion

The results of the examinations in patients with disturbances of the thyroid activity showed that such disturbances might exert an important influence on the temperature reactions of the fingers.

In some cases of *hyperthyrosis*, cooling of the fingers was impossible. If this statement is reversed a hyperfunction of the thyroid gland may be suspected if the fingers cannot be cooled in 20 minutes in water of 15° C. If the cooling is performed to the desired temperature, normal temperature curves can be expected as compared to the control material.

The cases of *hypothyrosis* showed that this disease may provoke all possible deviations from the ordinary course of the examination. For that reason the examination is of no value if there is a coincidence between myxoedema and some other disease to be investigated in this manner. In my opinion the diagnosis myxoedema must be excluded from every patient investigated on peripheral vascular disease either with plethysmography, calorimetry, thermometry or volume pulse determination. The differential diagnostic value of these methods will be dubious if a myxoedema is present.

The risk of faulty estimations of the examinations in peripheral vascular disease owing to disorders of BMR should not to be exaggerated. Manifest symptoms of such a disorder are necessary to influence the results of the temperature measurements in the present work. A thorough history will almost always be sufficient to exclude unfavourable influence of thyroid disease. It is noteworthy that all cases of *hyperthyrosis* clinically corrected to a normal state of metabolism at the same time obtained normal values in the temperature measurements. In contrast to this, the cases of *hypothyrosis* corrected, all showed some remaining deviations. Perhaps these were due to the increased tendency to contract arteriosclerotic disease, accompanying the myxoedema.

The material was considered too small to permit calculations between BMR and vascular reactions. In other respects the results were similar to those of authors cited. The opinion of Roth & Sheard (1950) that the basal heat production always must be considered in evaluating the results of skin temperature measurements was verified.

Summary

A material with manifest symptoms of disturbed metabolic rate was investigated with the method of reflex dilatation described and the results compared to those of the control material. *Hyperthyrosis* was accompanied either with a diminished ability to constrict the finger vessels in cold or an increased ability to dilate these vessels on heating the feet. *Hypothyrosis* was accompanied by a diminished ability to dilate the finger vessels on heating the feet. Successful therapy in *hyperthyrosis* was followed by a return of the vascular reactions to a normal state or even reactions similar to hypothyrosis. In *hypothyrosic* patients therapy could not produce a completely normal vascular reaction. It is emphasized that no examination on skin temperatures of the fingers may be evaluated without considering the thyroid function.

CHAPTER IV

PATIENTS WITH VASCULAR DISORDERS

A. Introduction

The material consists of six groups of patients. The division has been based on the following points:

1. Signs of complete or incomplete occlusion of some of the arteries in the arm.
2. Symptoms or signs of vasospastic disease without known origin (Raynaud's disease).
3. Sclerodermia of the fingers.
4. Symptoms or signs of vascular disease in the fingers associated with lupus erythematosus disseminatus (LED).
5. Vascular symptoms following cold injury.
6. Symptoms of vascular disorders associated with some neurologic disease.

The patients in Groups 1—4 consulted the doctors owing to the symptoms of vascular disease. This was also the case with some of the patients in Groups 5 and 6 (K 8, 9, 10 and N 9, 12). The other patients in Group 5 were intended as control subjects but referred to this group owing to the history. The remaining patients of Group 6 were subjected to the examination owing to the neurological symptoms.

The general clinical examination was the same as performed on the control subjects. The results were normal.

The examination of the vascular system included pulse palpation on arms and legs and oscillometric examination on both wrists and ankles. In no case these signs indicated pathologic circulation of the legs. The results of the arms are recorded in Table VIII.

Arteriography was performed in all cases where occlusive arterial disease was suspected. The artery was punctured at about the middle of the upper arm. The contrast medium injected was 35 per cent Umbradil.[1])

[1]) The roentgen examinations were performed at the Roentgen Department III, Sahlgrenska sjukhuset.

In some cases the constrictions observed appeared to be caused by muscular contraction rather than by organic changes in the vessel walls. An intraarterial injection of Priscoline (2-benzylimidazoline-hydrochloride) was then performed through the cannula and another arteriograph achieved.

B. Occlusive Vascular Disease

1. Material

This group was only composed of 8 cases: 6 females and 2 males (Table VIII.1).

Four of the female cases (O 3, 6, 8, 11) suffered from arteritis brachiocephalis (also called »pulseless disease» or Takayashu's syndrome, cf. Ask-Upmark & Fajers 1956). They will be published in detail by Welin (1957). The other two female cases manifested occlusions in the brachial artery, one after a recent embolus (O 10) and the other after some kind of arteritis. The male cases were victims to Buerger's disease with occlusions of both ulnar and radial artery of one arm (O 9) or only the one radial artery (O 5).

These patients had their occlusions verified by arteriography except for O 8 where one attempt failed and the patient refused to undergo further examinations of this kind, and O 10 where the diagnosis was considered as established by history and clinical signs. Her symptoms were, however, representative for the »pulseless disease».

There were thus four patients with symptoms and signs of occlusion of the main artery to the arm far from the fingers, one case with occlusion in the upper arm and two with occlusions in the forearm. One case had occlusions in both the upper arm and the forearm (O 1). She had suffered from occlusions of both the ulnar and radial arteries of that arm 6 years prior to the examination and had then had her index amputated because of gangrena. A year before the temperature examination she complained of accumulating vascular symptoms from the same arm. An arteriography then demonstrated an occlusion in the brachial but a recanalization of the ulnar artery.

The patients with »pulseless disease» had had symptoms during 2—21 years, the case of non-determined arteritis 6 years, the Buerger patients 2—4 months and the case of arterial embolus 1 month at the first temperature examination.

Oscillometry just above the wrist and pulse palpation at the radial and ulnar arteries revealed signs of impaired arterial circulation in 7 of the 8 arms (O 1, 3, 6, 10, 11) that were occluded above the elbow. In the eighth (O 8), where aortography had failed, oscillometry did not demonstrate any marked difference between the occluded and the unimpaired arm but the pulses were diminished on the affected side.

In the patients with arterial occlusion below the elbow (O 5, 9) the oscillometric readings were normal in both cases, but the pulses were diminished or absent corresponding to the affected arteries.

As regards other accompanying symptoms one female had attacks of fainting (O 6) probably due to constriction of the left carotid artery. No patient had any signs of localized damage to the central nervous system nor symptoms nor signs of heart insufficiency at the time of the temperature examination.

2. Results

Pathological temperature reactions of some fingers were found in 9 of the 10 hands where there were signs of occlusion somewhere in the arterial flow to the hand, if the first temperature examination on each patient was regarded.

In 6 hands of 4 patients (O 3, 6, 8, 11) the occlusion was distant from the hand (i. e. cases with »pulseless disease»). The number of pathological reacting fingers of these hands varied from 0—5. There was thus no real correlation between the presence of a proximal obstruction of the arterial supply and the finger temperature reactions.

None of these 4 patients had a complete occlusion of the affected arteries. There was no correlations between the width of the constriction as judged from the roentgenological examination, and the result of the temperature examination. The cases O 3 and O 6 e. g. showed approximately the same width of the constrictions in their 4 subclavian arteries, but the number of pathological fingers varied from 0 to 5. Case O 11 had a complete obstruction of the left subclavian artery and pathological temperature reactions only from two of the fingers of the left hand. Moreover, there were pathological temperature reactions noted from two fingers of the right hand of case O 11 where oscillometry and pulse palpation did not demonstrate any signs of vascular impairment. Arteriography failed, however, to verify the complete unimpairment of the corresponding subclavian artery. It must at once be emphasized that none of these four patients had any other signs of impaired circulation of the fingers and only one (O 3) had symptoms from the fingers, viz. a moderate sensation of cold.

The four cases with more distal occlusion of the arm arteries (O 1, 5, 9, 10) revealed a somewhat better agreement between the signs of vascular obstruction and the presence of pathological temperature reaction. There was always some pathologically reacting finger on each hand which had an occlusion in its arterial supply. These 4 patients had symptoms of vascular impairment from several fingers such as numbness, coldness and slight pain and signs mostly as discolouration. Ulcers and reduction of sensibility were not noticed. If only the first temperature examination is regarded in each case there is an

absolute correlation between the presence of symptoms and signs of impaired circulation of the fingers and pathological temperature reactions in cases O 5, O 9 and O 10. These three patients all had a history of less than four months. Case O 1 only demonstrated slight statistical deviations from the mean of the fingers (I b) which had symptoms of vascular impairment but a definitely pathologic temperature reaction of an adjacent finger. It, thus, behaves more like the cases of »pulseless disease» with lack of correspondence between symptoms and temperature reactions than the remaining cases of more peripheral occlusive disease. Case O 1 and the 4 cases of proximal occlusion all had a duration of disease of more than one year, whereas the other three cases had a duration of less than 4 months. It is possible that the *lack of correspondence between vascular signs and temperature reactions is due to the state of development of the collateral circulation rather than to the primary arterial obstruction.* This opinion is favoured by the decrease of symptoms accompanied by less pronounced temperature reactions, but unchanged results of pulse palpation and oscillometry at the wrist, noticed in cases O 5 and O 6 during the therapy.

Reactive hyperaemia during prolonged heating of the feet was applied to the arms of the cases O 9 and O 10 when they had failed to demonstrate any marked increase in temperature. There was a further increase in temperature observed, but neither rapid increase nor end temperatures above 32° C.

Ulnar nerve block was applied to the left arm of case O 6 at one examination. The anaesthesia was this time applied before cooling the hands; complete for the left little finger, and almost complete for the ring finger. Yet the fingers could be cooled to 16° C. After heating the feet the ring finger demonstrated a temperature reaction within normal ranges, the little finger showing only a short period of rapid increase and failed to attain an end temperature of 32° C.

Comments. The failure to attain an end temperature somewhat above 30° C on a finger tip after inhibition of the vasoconstrictor tone has been considered as a certain sign of the arterial circulation to the digit being obstructed somewhere (Ratschow 1953, Kramer 1956, Goetz 1956, Abramson 1956). In this investigation 32° C has been established as the lowest finger skin temperature which is compatible with a normal finger blood flow, after inhibition of vasoconstrictor tone. The series described of vascular occlusive diseases of the arm demonstrates that many patients can obtain a temperature above 32° C on the fingers of the obstructed area.

Two principal observations were made on the material of occlusive vascular disease:

1. Prolonged periods of latency were not observed in this group. When a rapid increase in temperature was seen, it occurred after a normal period of

latency. (If the narrower limits of 2 × S. D. had been preferred, only one finger would have had a prolonged period of latency).

2. In the majority of pathological observations it was impossible to attain a sufficient period of rapid increase in temperature or an end temperature above 32° C (I f, II a, II b and III). In the control material no observations of that kind were noticed. The few pathological reactions observed in the control material were of the I a—e type. For that reason the pathological reactions, classified I f—III, may be regarded as signifying definite pathological temperature reactions.

C. Vasospastic Disease of Unknown Origin

1. Material

This group included cases suffering from arterial disease presumably due to an increase in vascular tone, the origin of which was obscure (Table VIII.2). These disorders are generally classified as Raynaud's disease. Lewis (1930) and many with him believed that the constriction had originated in the arterial walls. Sunder-Plassman (1938) has reported inflammatory changes in the ganglionic cells of the lateral horn and the sympathetic chain in such cases, but these findings could not be confirmed by Craig & Kernohan (1933), Goetz (1956) and others. That the syndrome may have a cerebral origin will be further discussed (Paragraph G 3 of this Chapter). Cold haemagglutination is known to produce symmetric superficial gangrene in the digits and has been claimed as a cause of Raynaud's disease (Mc Combs & Mc Elroy 1937). Stats & Wassermann (1943), Sunder-Plassmann, Hillenbrandt & Schürholz (1954) and Goetz (1956), however, have not been able to demonstrate such haemagglutination in any case of Raynaud's disease. Leriche (1954) has summarized the knowledge of the origin of Raynaud's disease, as a reflex from the cold sensory corpuscles in the skin to the cutaneous vessels with only the peripheral parts of the reflex arch being known, not the central pathways and regulative centres.

Most authors seem to be of the opinion that an increase in vasoconstrictor tone constitutes the origin of the attacks of pallor, numbness, cyanosis and gangrene of the finger tips. Secondary to the attacks of arterial constriction there will sometimes be hypertrophy in the muscular wall of the digital arteries, intimal proliferations and thrombosis (Lewis & Pickering 1934, Lewis 1938). This secondary, occlusive disease of the vessels, is considered to cause gangrene of the finger tips. The tendency to vasoconstriction is not limited to the arteries, but is also found in the venous part of the circulation. This venous implication decides whether cyanosis will occur or not in the digits after the initial phase of pallor (cf. Goetz 1956 for a more detailed description).

All cases in this group had attacks in the fingers of numbness and changes in colour, elicited by cold or emotional stress. The symptoms were symmetrically distributed to all fingers. There was no clinical evidence of occlusive disease in the major arteries as the oscillometric readings and pulse palpations at the wrist were always normal. All cases where some probable cause of the vascular disorder such as neurological disease, frostbite etc. could be established, were referred to these groups, although the vascular symptoms were identical with those of Raynaud's disease. The necrotic lesions had been limited to the skin of the fingers. All these patients except three (S 10, 35, 47) had suffered from their disease for more than two years.

The cases in the present series therefore fulfil the criteria for Raynaud's disease demanded by Goetz (1956) except the three with a history shorter than two years. Mendlowitz (1954), Allen, Barker & Hines (1955) and Abramson (1956), however, demand a cyanotic phase following the initial pallor for a diagnosis of Raynaud's disease. I have, therefore, classified the patients without cyanotic phase as cases with »dead fingers» and the others as true Raynaud's disease. Two of the cases with short duration (S 10, 35) were referred to the first group and one to the second (S 47).

2. «Dead Fingers«

This group included 7 cases: 6 females and 1 male (Table VIII.2 a). Heredity of the disease was reported by two patients (S 29, 35). The attacks of pallor were always elicited by cold never by emotional stress, but two of the patients (S 10, 12) admitted continuous nervous stress. One patient had hemicrania (S 35) without connection to the finger symptoms. As for coincident symptoms of impaired vascular function one patient suffered from cold cyanotic feet (S 29) and another from cold cyanotic knees (S 41).

The temperature curves of the fingers were interpreted as normal (as judged from the control group) in 4 of these patients (S 24, 29, 35, 41). Two of them (S 10, 46) displayed values for all the measured variables, which were individually normal but statistically deviating more than $3 \times$ S. D. from the other fingers (I b). It has been mentioned before in Chapter II that deviations of this kind are classified as probably normal. Only one female (S 12) did not attain normal end temperatures on four fingers while all other variables were normal.

3. Raynaud's Disease

This group included 20 cases: 14 females and 6 males, varying in age between 24 and 54 years (Table VIII.2 b). Heredity to the disease was admitted in three cases (S 4, 5, 30). Four of the patients had similar troubles from their feet as from their hands (S 5, 17, 31, 43). Two of them suffered from continuous nervous tension (S 16, 17).

The attacks of pallor and numbness were elicited by cold air and water in all cases except one (S 11), where the provoking agent was cold wind only. Some of the patients with long duration of the disease had their attacks elicited also from air of 20° C i. e. ordinary room temperature (S 1, 15, 18), change in temperature from warm to cold or vice versa (S 32) or even from a warm hand bath (S 5). Only one patient admitted that attacks were also provoked by emotional stress.

All fingers were involved in all patients. The part of the fingers that became pale and numb was never less than the two distal phalanges of the fingers and the distal phalanges of the thumbs. Sometimes the symptoms and signs were extended to the middle of the metacarpus, and in one patient to the middle of the forearm (S 16).

There were no necrotic lesions seen at the time of the temperature examination but 5 patients had scars on their finger tips (S 3, 8, 21, 38, 47) and one suffered from recurrent paronychial infections (S 2). One of the patients with scars had calcinotic incrustations in the finger tips in connection with the scars and also an incrustation on the left elbow (S 8).

The temperature examinations revealed normal reactions in 5 cases (S 4, 5, 17, 18, 32). Two more patients showed only the statistical deviations (I b) regarded as probably normal (S 3, 16). Thirteen patients of this group, in which all the males were included, demonstrated temperature curves of the fingers with courses that were not observed in the control group.

Prolonged periods of latency (I c) appeared in 8 of these patients (S 1, 2, 8, 11, 21, 31, 36, 40). In 46 of their fingers, the prolonged period of latency was the sole deviation from the normal course, and in 5 fingers it was combined with some other abnormality of temperature reaction (I d, I e, I f). The prolonged periods of latency usually did not exceed 40 minutes, but in two cases values of 49 (S 30) and 60 minutes respectively (S 11) were obtained. Six of these patients had also one finger or more that failed to attain a temperature above 32° C at the experiment (S 1, 8, 11, 21, 31, 36).

Too long periods of rapid rise (I d) and a too small increase in temperature (I e) were seen only in 4 fingers on three of the thirteen patients (S 1, 8, 47).

Rapid increase in temperature followed by failure to attain a temperature above 32° C (I f) was observed on 7 fingers of 4 patients if only the first examination was considered (S 11, 15, 21, 31).

Slow increase in temperature with an end temperature above 32° C (II a) appeared in three cases (S 1, 8, 47) and the same course with failure to attain this temperature in five (S 1, 8, 30, 38, 47).

No apparent increase in temperature was manifested in any fingers of S 30 and S 43 and in 1—3 fingers of S 21, 31, 36.

The only signs of vascular damage that could be relied upon in these patients was the presence of scars on the digital ends. If the distribution of

scars on the fingers was compared with the distribution of vascular reactions there was correlation between the presence of scar and the disability to attain 32° C end temperature only on 7 fingers from 4 patients (S 8, 36, 38, 47). Most of the other scarred fingers had shown normal or almost normal temperature reactions or some of the abnormalities with an end temperature within the normal ranges.

Repeated examinations were performed in three cases. In case S 47 there was only one week between the examinations. The right ring finger failed to attain tolerable end temperature at both examinations. In the first examination there were two other fingers displaying abnormal reactions Owing to this failure to attain tolerable end temperature, an arterial obstruction was suspected and an arm arteriography was performed on the right side. The arteries of the fingers were narrow and some of them were not filled with contrast medium. The picture appeared to be rather typical of Raynaud's disease as described by Steiner (1956).

Case S 11 was examined twice with an interval of about one year. At the first examination she had severe attacks in her fingers so that she must be hospitalized because of the pains. All ten fingers were abnormal according to the temperature examination. At the second examination she had hardly any complaints perhaps because of intensified therapy. There was still one finger deviating from the control results, but the other fingers were completely within the limits.

Case S 30 was examined twice with one year's interval. No finger obtained tolerable end temperature at any of the examinations. His complaints were the same at both examinations.

Reactive hyperaemia was induced in 5 cases where 35—40 minutes of heating of the legs had failed to induce tolerable end temperature in all fingers. In the cases S 11, S 36 and S 43 a rapid increase in temperature was provoked to end temperatures above 32° C. In case 38 the increase in temperature was not rapid, but end temperatures above 32° C were also obtained. In case S 30 there was a rapid increase only in two fingers of the examined right arm, but the cuff had been applied erroneously to the upper arm and most of the provoked increase in blood flow probably went to the muscles of the forearm.

Ulnar nerve anaesthesia was applied to the left arm of the patient S 30 on the same conditions. A rapid increase in temperature to an end temperature above 30° C was seen in the anaesthesized little finger.

4. Discussion

As judged by the results of the temperature examinations in the present manner there is no reason to separate the group with »dead fingers» from the group called Raynaud's disease. In the first group there was one case

with failure to attain tolerable end temperatures on 4 fingers and in the second there were 7 patients who displayed normal (or almost normal) temperature curves on all fingers as judged from the control material. If the frequencies of normally reacting individuals in the two groups are compared by a χ^2-calculation there is no significant correlation ($0.10 > P > 0.05$). According to the present investigation the appearance of a cyanotic phase after the attack of pallor and numbness does not with certainity indicate a more severe degree of vascular impairment.

It must be emphasized that the present material contains no patient with really severe damage to the finger ends. Necrotic lesions had been observed, but they were all healed at the time of the examination. This fact is perhaps due to the circumstance that all patients with long duration of the disease had been subjected to continuous therapy. The material for that reason is not representative for all manifestations of Raynaud's disease.

The patients in these conjoined groups of vasospastic disease all had symptoms from all fingers, and the symptoms were evenly distributed to all fingers. Only the patients who had fingers with scars could be classified as having had more marked symptoms from these fingers.

There were thus many fingers that showed symptoms of impaired circulation, but no signs according to the present method of examination. I am inclined to interpret this discrepancy as due to the functional nature of Raynaud's disease, i. e. that the disease is not distinguished by the presence of vascular obstructions.

There were, however, patients who had scars on the finger tips as a possible sign of vascular obstruction. I have already stated, that the conformity between the situation of the scars and the ability of the finger to attain a tolerable end temperature was not marked. There was no correlation between the fact that the finger was subjected to scars and severe and moderate impairment of the temperature reaction within the 5 patients having scars ($0.30 > P > 0.20$). This fact is comprehensible as the scars were the residues of previous grave stages of the disease and did not signify the state of circulation at the temperature examination.

It is remarkable that all fingers attained an end temperature above 32° C when reactive hyperaemia or anaesthesia by ulnar nerve block was properly performed as a complement to the reflex vasodilatation.

D. Disseminated Lupus Erythematosus

Systemic lupus erythematosus is regularly classified in the group of collagen diseases. Guion & Adams (1943) demonstrated that the small arteries and arterioles were damaged in different parts of the body. This damage con-

sisted of proliferation of the connective tissue in all layers of the vessel most apparent in the subintimal layer and the adventitia. There was also a deposition of homogeneous eosiniphilic material in the vessel walls associated with fibroblastic proliferation. This reaction may lead to narrowing of the lumen and sometimes complete obstruction of the vessel (Abramson 1956). Pallor and cyanosis of the fingers commonly accompany this disease and according to Goetz (1956) Raynaud's syndrome may precede the outbreak of the systemic lesion for several years. Goetz observed that the onset could appear in connection with a sympathectomy and for that reason recommends all cases of Raynaud's disease to careful examination aiming at the exclusion of systemic lupus erythematosus especially if operation is planned.

The material includes three cases of disseminated lupus erythematosus with symptoms of vascular diseases in the fingers (Table VIII.3). All are women aged between 30 and 53 years. No history of heredity was obtained. The duration varied between 1 and 15 years. In 2 cases the vascular symptoms had appeared some time after the onset of the lupus. One case (S 44) had had dead fingers for 9 years preceding the LED. The puls and oscillometric readings at her wrists were all normal. The case of 15 years' duration had had pallor of her fingers for 10 years and ulcerations the last three years before the temperature examination. The ulcerations had healed on treatment with 1 per cent cortisol (hydrocortisone) ointment but returned each time the treatment was interrupted. At the time of the examination she had scars and defective nails on the tips of the right index to little finger and the right ring finger. The temperature examination showed very prolonged periods of latency in eight fingers 54—67 minutes followed by a normal increase in temperature in all but one. In four fingers the temperatures were normal. Only one finger did not show any increase in temperature.

The second case (S 34) had had recurrent symptoms of discoid lupus on her legs for 7 years, sometimes with ulcerations. She had also had migrating pains and swelling of the joints. The last year she had suffered from pallor and cyanosis of her fingers, provoked by cold air and cold as well as warm water. There were no scars. The temperature examination showed normal results in eight fingers and failure of two to reach end temperatures above 32° C. Reactive hyperaemia was provoked, but did not give any further increase in temperature.

The last patient in this group had had typical lupus erythematosus manifestations since one year in her face and on her hands. Her joints had been tender, swollen and stiff sometimes. She had suffered from pallor of her fingers on her right hand for ten years without cyanosis or scars. Temperature examination showed normal curves of all fingers.

E. Sclerodermia

Sclerodermia of the fingers almost always demonstrates Raynaud's syndrome during some period in the progress of disease (Rossier & Hegglin-Volkmann 1954). There has been divergent opinions whether the attacks of vasoconstriction cause the sclerosis or are secondary to it. Recent authors are of the opinion that sclerodermia is the primary disease if there are sclerotic changes in the visceral organs or other parts of the skin than the fingers and that Raynaud's disease might be followed by sclerosis which is limited to the fingers (Allen, Barker & Hines 1955, Goetz 1956, Ratschow 1956). Abramson (1956) and Martin (1956) place the primary sclerodermia in the group of collagenosis. Whether the sclerosis of the fingers is primary or secondary it is generally preceded by a period of attacks of pallor and cyanosis in the fingers. According to Martin this period does not exceed 5 years. Patho-anatomical investigations show a widespread fibrosis in the fingers that compresses the digital vessels. On roentgen examination segments of complete vascular obliteration appear in the finger arteries that are similar to those seen in cases of Buerger's disease (Martin 1956). Cutaneous sclerosis is observed in the face, back, elbows, thighs and more seldom feet. Oesophageal constrictions are rather common, sclerosis in other organs as lungs and liver more rare.

The present material includes 4 cases of sclerodermia, three men and one woman (Table VIII.4). They had all had attacks of pallor and cyanosis of the fingers prior to the sclerotic changes. Their age varied between 37 and 66 years and the duration from 2—19 years. All had sclerotic skin manifestations on other parts of the body. Three of the patients had scars on all finger ends, the 4th only on the thumb and little finger on both hands (S 26). One patient (S 37) also had benign diabetes after an operation for pancreatitis. He was treated with diet only. He also suffered from alcoholism probably secondary to the digital symptoms that were relieved by alcohol consumption. None had any signs of involvement of the large arteries as judged by pulse palpation and oscillometry at the wrists. Two cases had a marked heredity for Raynaud's disease.

Case S 37 showed a normal temperature curve on one single finger. All other fingers of these patients showed hardly any or no increase at all in temperature (III). In two of the cases the examinations were completed with reactive hyperaemia and ulnar nerve block. Only a slight increase in temperature was observed.

Arteriography of one arm was performed in three of the cases (S 9, 25, 37). All these showed atrophy in the end phalanges of 4 or more fingers on both hands. Arterial filling was not attained in the fingers of S 9, S 25 or the hand of S 37. On two of the angiographs (S 9, 25) several circumscript constrictions in the main arteries of the forearm were observed. A cold hand

bath was performed on case S 9 followed by another injection of contrast dye. After that the constrictions were more pronounced and no filling could be seen of the vessels of the hand. In the cases S 25 and S 37 Priscoline was injected into the arteries prior to a second injection of contrast medium. All arteries were more dilated after this injection, the contrast medium was seen also in the finger tips, and the constrictions seen in the arteries of case S 37 had vanished except one in the radial artery near the elbow which was less marked. (These cases will be reported in detail by Bartley and Lindqvist 1957.)

Discussion

The vascular impairment in cases of sclerodermia seems to be more complicated than has been believed before. In two of the present cases (S 9, 25) the roentgen examination revealed constrictions in the arterial walls that were similar to organic occlusions but could be increased by cooling and relieved by Priscoline injection. No sure persistent occlusion of the finger vessels could be observed but the finger vessels could not be visualized without injection of a dilatating agent. As far as I have found such proximal constrictions have not been observed earlier in cases of digital involvement by generalized sclerodermia. According to arteriography in the present cases an occlusion causing the signs of digital necrosis must be situated in the minute vessels in the immediate vicinity of the tissue damage. For that reason it seems more probable that the arterial constrictions observed caused the failure of digital circulation in cases S 9 and S 25. *Thus sclerosis of the finger tips might be secondary to arterial constrictions, also if there are sclerotic changes elsewhere in the skin.* The segments of obstructions observed in the finger arteries by Martin might be constrictions.

F. Cold Injury

According to Schumacker and Lempke (1956) the most significant sequela of frost-bite, other than loss of tissue, is sympathetic overactivity. Allen, Barker & Hines (1955) stated that Raynaud's syndrome may appear subsequent to a frost-bite. Martin (1956), however, held the opinion that this type of Raynaud's syndrome is the result of an endarteritis in the vessels subjected to persistent or severe cold. Ratschow (1953) considered the sequelae of frost-bite as an increase in sensitivity to cold, but did not enter upon the precise meaning of this statement.

In the present material one patient (K 8) was examined within one month after a cold injury (Table VIII.5). After the frost-bite he had suffered from blisters on all the finger tips of his right hand and the two ulnar fingers of his left.

There was a little necrosis ulnarly on his right little finger. At the time of the temperature examination there was dry and light brown skin of the distal phalanges of the fingers mentioned, but no loss of tissue or of sensibility. The temperature examination showed no increase in temperature on the two right ulnar fingers and normal reaction of the others. Reactive hyperaemia was applied after 37 min. of leg heating. The ring finger then showed a slow increase up to 24° C in 30 min. but in the little finger there was no increase. Two months after the examination he was free from symptoms and refused further investigation.

Another patient (K 10) had contracted a frost-bite on a winter sailing to Murmansk. The frost-bite was followed by attacks of pallor, numbness and cyanosis of his fingers provoked by cold air and water. At the first temperature examination, two years after the beginning of the disease, he showed various deviations from the normal as seen in the table, but end temperatures above 33° C were attained in all fingers. Two years later his symptoms were more pronounced, perhaps because he had omitted therapy. There were, however, no signs of necrosis or other trophic disturbances of his finger ends. At that time all fingers showed normal periods of latency and rapid rise and normal increase in temperature during the period of rapid rise. Tolerable end temperatures were, however, not attained on any finger. Reactive hyperaemia was provoked but only a slight further increase in temperature was recorded to temperatures between 31 and 32° C.

One other patient (K 9) had had symptoms for 13 years after an old cold injury and showed prolonged periods of latency in three fingers. She had, however, lymphoedema of the lower legs and perhaps the circulation in the legs was so impaired as to influence the results of the temperature examinations.

The seven remaining patients in this group had had their cold injuries 5—35 years prior to the examination. They differed from the patients otherwise mentioned in the series of vascular disorders as they had no definite symptoms of vascular disease. Most of them had some irritation in the finger tips in cold, only one (K 7) suffered from somewhat pale fingers in cold water. Two of these cases showed completely normal temperature curves, the others had deviations of the types I a and I b in the temperature curves of rather many fingers.

Comments. The three cases with symptoms of vascular injury were too few to signify the appearance of the temperature reactions in cases of cold injury. The seven cases without marked symptoms might indicate that the small intervals in the rapid increase of temperature and the statistical deviations between otherwise normal reacting fingers which were noticed in the control series were possibly secondary to old forgotten cold injuries.

G. Neurologic Diseases

The inhibition of the vasoconstrictor tone studied in the present investigation must be influenced by neurologic disorders affecting the cerebral centres of vasomotor regulation or the neural pathways for the constrictor impulses. Some selected cases of various nervous diseases were therefore examined to illustrate this influence (Table VIII.6). These cases have been divided into three groups:

1. One patient with traumatic peripheral nerve injury.
2. Six patients with neurological symptoms of the arms, probably due to cervical nerve root affections.
3. Two patients with histories indicating previous encephalitis.

1. Case of Nerve Injury

This patient (N 6) had contracted a wound from a glass splint on the right wrist cutting his median nerve. There was paresis in the right abductor and opponens of the thumb and loss of the power of sweating in the three radial fingers. The temperatures of the fingers before and immediately after cooling did not show any difference between the hands (about 30° and 15° C respectively).

On heating the feet there was a normal increase in temperature in the left hand and the two ulnar fingers of the right as compared to the control results. The right thumb produced a normal temperature curve too with a period of latency, that was within the normal ranges 3 × S. D., but prolonged as compared with the periods of the seven fingers rising normally in temperature. The right index and middle finger did not show any increase in temperature within 40 minutes. After that time reactive hyperaemia was induced in his right arm but no increase in temperature was seen either.

Comments. This case is considered to demonstrate the secondary stage of increased vasoconstrictor tone that follows two weeks to several months after a nerve injury. According to Lynn (1956) the increase of vasoconstrictor tone is not relieved until the sensory nerve fibres have regenerated and for that reason skin temperature and blood flow will not respond to body heating but only to reactive hyperaemia. In this case, however, there was no response to reactive hyperaemia either. The significance of this lack of response remains obscure. Some injury of the vessels to the hand at the place of the wound was not probable because 1) the pulses at the wrist were normal, 2) the thumb showed a delayed but normal temperature reaction, 3) the temperatures of the two fingers that did not react, were above 30° C before cooling in spite of the room temperature of 15° C.

2. Cases of Cervical Nerve Root Affections.

Patients with affections of the nerve roots often have a sensation of cold in the affected extremity (Lewis 1936, Ratschow 1953). In the present material, neurological symptoms or signs of some arm in five patients were probably secondary to degenerative lesions of the cervical intervertebral discs. Another had similar symptoms and signs but no disc degeneration visible on roentgen examination.

Two of the patients with disc degeneration only complained of a feeling of cold and pain in the affected arm. Their temperature reactions were normal.

The four cases with neurological signs (N 1, 2, 3, 7) had slight paresis in various muscle groups of the arms besides the feeling of cold. Only one had impairment of sensibility (N 2). Two of them (N 1, 3) had no abnormalities in finger temperature curves. Another (N 7) was troubled with her right ring and left index fingers that were white and cold if exposed to cold air or water. These two fingers showed a phase of rapid increase in temperature but the latency periods were about 20 minutes longer than those of the other fingers, and these two fingers also failed to obtain an end temperature of 32° C. The fourth case (N 2) suffered from paresis in some muscles of his left arm and a decreased pain sensibility in the ulnar part of his right hand and forearm. In his left arm there was a rapid phase of increase in temperature in all fingers but the latency periods were 36—39 minutes and only one finger could obtain the end temperature of 32.1° C. The fingers of his other hand showed only a slow increase up to temperatures of 26 to 29° C .

Comments. This group was rather small. The results of the examinations can, however, reveal that cases of disc degenerations, without signs of neural involvement, may have normal temperature reactions in the fingers. In cases of nerve root injuries showing signs of motor nerve involvement only, there may be pathological temperature curves from the fingers, and if there are signs of disturbed sensibility in the hands or cold white fingers the temperature reactions are probably abnormal as compared to the controls. This is in line with the report of Allen & Craig (1938).

3. Cases with Postencephalitic Cerebral Lesion

Vasomotor symptoms in patients with cerebral affections are not uncommon, especially secondary to vascular lesions (Vanggaard 1941, Lund 1944). Raynaud's syndrome as a probable sequela to an encephalitic process has not yet been described as far as I have found.

Two of the patients stated histories which presumably indicated attacks of encephalitis some years prior to the examination.

The first patient (N 12) in 1952 was taken ill with vertigo, headache and a

feeling of stiffness in the right side of her face, her right arm and leg. She did not show any signs of neurological disease at the usual examination and lumbar puncture, pneumoencephalography and carotid arteriography were normal. The electroencephalography demonstrated, however, a focus in the right postcentral region at two examinations with 4 months' interval. After this incidence she suffered from attacks of pallor and numbness in her fingers. At a temperature examination 1954, she revealed pathological temperature curves on all fingers but normal end temperatures were always attained. In 1956 when the attacks of white fingers had become rather infrequent she showed intervals of 1—3 minutes in the phase of rapid increase on four fingers of her left hand but the temperature curves were otherwise normal.

The second patient (N 9) had had a severe encephalitic process 15 years prior to the first examination. After this disease he suffered from tremor in the right half of his body and a permanent feeling of cold interrupted by attacks of pallor, cyanosis, and numbness in his right hand and foot, provoked by cool air and water. He was submitted to 4 temperature examinations in the course of one year. No obvious increase in temperature was induced in the fingers of his right hand by warming the feet at any examination. He had no symptoms from his left hand, but some fingers still showed pathological temperature curves at a minor degree as compared to the right. An attempt to induce reactive hyperaemia in his right hand after 32 minutes of heating gave no further increase in temperature. An ulnar nerve block was applied 22 minutes later and was followed by a slow increase in temperature in his two ulnar fingers that commenced within ten minutes, at the same time as the anaesthesia was completed. The anaesthesial agent, however, diffundated to the median nerve as well. At the same time as the anaesthesia was complete on the volar surface of the finger tips their temperatures also commenced a slow increase. All end temperatures attained or surpassed 33° C.

Comments. Peet & Kahn (1936) have reported a case of hypothalamic tumour where the patient developed severe vasoconstriction of the extremities and the clinical picture simulated Raynaud's disease. Lindqvist (1950) has reported a similar clinical picture following head injury. The case last described here indicates that an encephalitic lesion in the basal parts of the brain as manifested through the tremor, may also cause an increased vasomotor tone in the fingers, which may be released if the peripheral pathways for the constrictor impulses are blocked. This person had abnormal temperature reaction also from the other side of the body where no neurological signs were observed. The other patient developed symptoms of vascular disorder after more or less significant symptoms of encephalitis. These two cases may illustrate that also cerebral processes which heal with slight symptoms might cause a disorder in the vasomotor tone.

H. General Discussion of Results in Patients with Symptoms of Vascular Disorders

In the textbook on vascular disorders edited by Samuels (1956) e. g. Kramer and Perilstein state: »It is obvious that the skin surface temperature procedure not only helps to determine the underlying cause of the impaired circulation, but also gives information of the relative degree of occlusion and arteriospasm».

Goetz, however, in the same book mentions that »The high vasomotor tone recorded between the attacks may be so persistent that it cannot be relieved by reflex body heating, the vessels dilating only with local application of heat». He observed about 20 cases of Raynaud's disease out of 120 where the skin temperatures of the digits attained 32° C after 30 minutes of reflex body heating, while plethysmographic readings demonstrated interference with the blood flow up to 50 per cent of normal. One author considers the skin temperature measurements during reflex vasodilatation as reliable and the other believes that they are misleading in about 16 per cent of the cases. This disparity is rather great. Goetz does not seem to display any interest in the course of the temperature curves, only of the maximum temperatures attained within 30 minutes. It is possible that some of the patients with misleading results had demonstrated a pathological increase in temperature, had the temperature been measured more frequently. When the temperature measurements are too sparse some of the features of the curves may be missed such as I d, I e and II a. Curves with these abnormalities will most probably be judged as normal and thus give a false result of the examination. If the time of the heating were restricted to 30 minutes according to Goetz (1956) all the cases of prolonged period of latency in the present investigation would be judged as showing no tendency to dilate, and some of the controls with a period of latency close to the upper limit of 30 minutes would be judged as pathological. If the opinion of Goetz seems to involve an underestimation of the diagnostic possibilities of the skin temperature measurements at reflex vasodilatation, the statement of Kramer & Perilstein quoted, seems to be an overestimation as will further be discussed.

To test the value of the present procedure of investigation in distinguishing fingers with normal from abnormal circulation, calculations were made on the whole vascular material conjoined.

According to history and results at the clinical and roentgenological examination three degrees of *vascular impairment* were created.

1. *No impaired circulation* (No), i. e. the fingers did not demonstrate any symptoms or signs of vascular disorders.

2. *Slightly impaired circulation* (Sl), i. e. symptoms of impaired circulation were present but the patient was not restricted in his usual activities such as washing or outdoor work.

3. *Seriously impaired circulation* (Se), i. e. the patients were restricted in their usual activities by vascular symptoms of their fingers or demonstrated signs of actual damage to their finger tissues.

This classification referred to the state of the fingers at the temperature examination and the history of the preceding weeks. Healed scars on the finger tips e. g. were not supposed to indicate the state of circulation at the moment of the temperature examination.

The results of the *temperature examinations* were also classified in three degrees, fingers with:

1. *Normal temperature reaction* (N), i. e. the temperature curve of the finger is within the limits 3 × S. D. calculated from the control material, or shows the deviations from these limits called I a and I b, which are considered as not truly pathological.

2. *Moderate pathological temperature reactions* (M), i. e. all other temperature curves with an end temperature above 32° C, the minimum temperature considered as normal in the present investigation. That is the deviations from the control limits 3 × S. D. called I c, I d, I e and II a.

3. *Severely pathological temperature reactions* (S), i. e. the curves which do not attain 32° C, the deviations I f, II b and III.

The fingers were regarded individually and tabulized according to these two reasons of classification (Figure 3). A χ^2-calculation demonstrated that there was a highly significant correlation between the impairment of circulation and the degree of vascular reaction ($0.001 > P$). Only the first examination on each patient was used in this calculation. The fingers of one person, however, are not independent of each other. If this connection is regarded, the correlation is still highly significant.

There were, however, fingers with normal circulation according to history and clinical examination that demonstrated pathological temperature reactions and vice versa. *For that reason the practice to judge the circulation of the fingers from the result of one single finger or one finger of each hand must be hazardous if no cautions are taken to ensure that the fingers investigated are representative of the impaired state of circulation.* The history and the result of the clinical examination is most often, but not always an indication as to which finger is suited for the examination. There may be severe symptoms indicating vascular impairment as in some cases of neurological or »spastic» vascular disorder where no signs of impairment are to be found. There may also be a lack of symptoms as in some cases of occlusion where there are profound signs of impaired circulation. The group of patients with symptoms of vasospastic disease may illustrate this statement. There were 27 patients in this group and 25 of these had actual symptoms of disease from all fingers. If the estimation of the finger circulation was made on all 10 fingers, according to the present investigation, 14 individuals were judged as abnormal. If the fingers

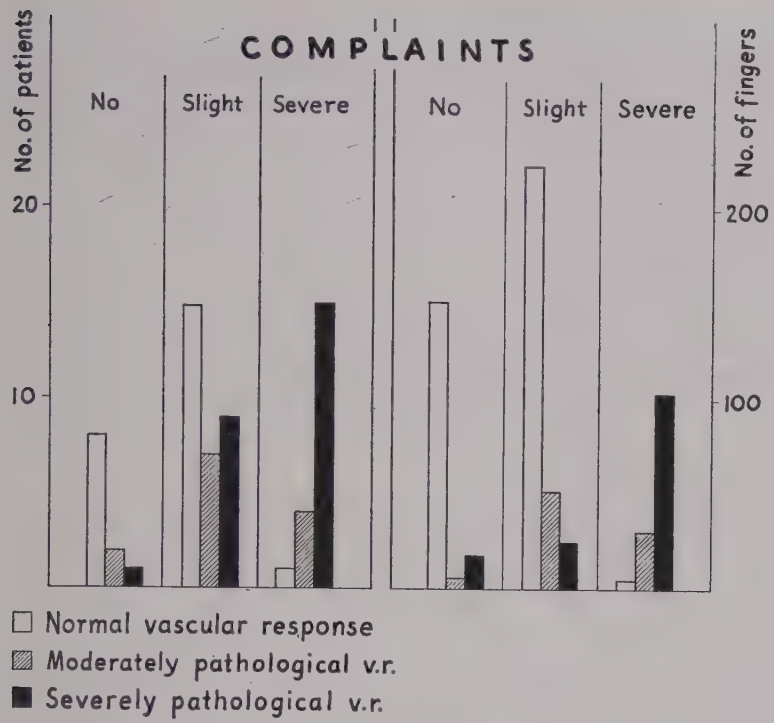


Figure 3. Correlation between the degree of complaints and the degree of temperature reaction. In the right part of the figure the patients of the conjoined groups of vascular disorders are tabulized according to the finger with the most pronounced reaction. In the left part the complaints and the mode of reaction are studied on each finger of these patients.

were used one by one to determine the number of abnormal individuals this number varied between 9 and 13. The chance to make a correct estimation naturally increases with the number of fingers examined. It must, however, be admitted that in the present group of patients with vasospastic disease, the examination of the thumb, the middle and little fingers on each hand (as Heidelmann 1951) would have given a congruent result to the examination of all fingers as regards the classification of the patients.

The patients were also classified according to the symptoms and signs in the most impaired finger (Figure 3). The result of the temperature examination from the finger with the most accentuated reaction was then correlated to the above group. There was a highly significant correlation ($0.001 > P$).

Failure to attain a temperature higher than 28—29° C on the finger ends after reflex vasodilation has been considered as indicative of occlusive vascular disease (Kramer & Perilstein 1956). In the present investigation ulnar nerve blocks were applied in some cases where heating of the feet had failed to induce an increase in temperature compatible with the demands on the controls.

In two of these (S 30, N 9) the block of vasoconstrictor impulses produced a further increase in temperature of the anaesthesized fingers to values above 33° C. The failure to attain end temperatures above 32° C in these cases with solely heating of the feet most probably was not due to an arterial occlusion but to an increase in vasoconstrictor tone.

I therefore agree with Goetz (1956) that there is no possibility to differ distinctly between occlusive and so-called functional vascular disease by reflex vasodilatation alone.

In my opinion the results of the present method of investigation may only be interpreted as representing the capacity of the fingers to restore the blood circulation after a vasoconstriction has been induced. In subjects with normal finger circulation this restoration is always attained by heating the feet in water of 42—44° C and the increase in temperature follows in curves within the limits stated (Chapter II C).

If the finger circulation is impaired the increase in temperature may deviate from this standard course of the curve or fail to attain a tolerable end temperature whether the impairment is due to occlusion or increase in vascular tone. A successful supplementary ulnar nerve block or reactive hyperaemia giving an increase in temperature indicates that the vascular tone of the fingers was not abolished by the heating of the feet alone. There might, however, still exist an occlusion with well developed collateral circulation which will supply enough blood to permit a rapid increase in temperature when the vascular tone is relieved. If nerve block or reactive hyperaemia are technically correct but the increase in temperature fails to appear, an arterial occlusion is more probable, but there might also be infiltrations in the walls of the terminal vessels (i. e. arteriolar, capillary and venular), which cause the lack of vascular response.

For reasons mentioned the present method of investigation should not be relied upon as the sole method in establishing the differential diagnosis of vascular disorders. The history, the clinical examination including observation of the skin, pulse palpation etc. and the arteriography must always be taken into consideration and often give more valuable information. The temperature examinations may give supplementary information about the range of functional variability in the finger end circulation.

There are, however, some features of the temperature curves which may be mentioned as probably indicative of occlusion or not.

In no case of verified vascular occlusion a prolonged period of latency was the cause of judging a finger as abnormal. If there was any increase in temperature, it either commenced within the control limits $3 \times$ S. D. and the following increase was too slow (I d) or too small (I e, I f), or the increase in temperature started about the same time as in the hand with unimpaired circulation, but was slow during the whole examination (II a, II b). This observation is in line with the observations of Lindqvist and Sigroth (1952) on toes.

On the contrary, prolonged periods of latency were frequently observed on the fingers of patients with diseases where an increase in vasoconstrictor tone was supposed to cause the symptoms and signs. Thus prolonged periods of latency indicate the presence of functional vascular disease probably secondary to an increase in vascular tone.

In case of occlusive vascular disease the abnormal temperature reactions seem to be limited to the fingers with symptoms and signs, if the occlusion is distal to the elbow. In disorders of the vasoconstrictor tone, fingers with abnormal temperature reactions may be observed side by side to normal fingers with long periods of latency besides such with short, and all these fingers may have about the same symptoms or even the abnormally reacting finger have less symptoms than that reacting normally.

I. Signification of the Courses of the Temperature Curves

1. The Signification of the Variables

As stated in Chapter I 13, the temperature curves were divided in a period of latency, a period of rapid rise in temperature and at last, a period where the curve was less vertical, and attained a maximum temperature called end temperature. The functional signification of these variables will now be discussed. (Cf. Figure 1, page 10, and Figure 2, page 39.)

According to Clark (1938) and Vanggaard (1941) the cutaneous arteriovenous anastomoses are extensively supplied with vasoconstrictor fibres predominantly controlled from the hypothalamic heat loss centre. The constrictor fibres exert most of the control of these vascular formations. The arteriovenous anastomoses are especially numerous in the digital ends (Grant & Bland 1929/31, Clara 1956).

A period of rapid rise in temperature on the finger end, therefore, probably indicates the opening of the arteriovenous anastomoses and is secondary to a decrease in vasoconstrictor tone (Vanggaard 1941). The periods of rapid rise defined in the present investigations plausibly indicate the same phenomena. The variables, period of rapid rise and increase in temperature, constitute two possibilities of this increase in temperature to deviate from the normal and are calculated separately only because there is no statistical correlation between them.

The period of latency is defined as the time between the commencement of the heating and the beginning of an increase in temperature of more than 1° C a minute. A slight increase in temperature frequently appears during some minutes before the rapid rise begins. This rise in temperature probably indicates an increase of the blood perfusion of the finger end. It is not possible to determine if this perfusion is capillary or if it is secondary to a slight decrease

in the tone of the arteriovenous anastomoses. A prolonged period of latency (I c) plausibly indicates an increase in vasoconstrictor tone. This assumption is confirmed by the behaviour of the temperature curves in some cases of Raynaud's and neurological diseases. If the prolonged periods of latency are followed by completely normal curves, this indicates 1) a normal power of the arteriovenous anastomoses to dilate, 2) an unimpaired supply of blood through the arteries.

To fulfil the demands on the end temperature only a rather small increase in the blood flow of the finger end is necessary (Goetz 1956). *Only the combination of an acceptable period of rapid rise in temperature and a sufficiently high end temperature may therefore be accepted as indicating a normal blood supply to the finger end.* A failure to attain end temperature above 32° C must be regarded as a sign of rather severe impairment of the circulation in the finger end either after a normal period of rapid rise (I f) or not (II b). A slow rise in temperature to an end temperature compatible with normal circulation (in this work minimally 32° C) indicates either a loss of the power of the arteriovenous anastomoses to dilate (through increase in vasoconstrictor tone or infiltration of the vessel wall) or an impaired arterial supply.

2. The Signification of the Possibilities of Deviation from the General Appearance of the Temperature Curves

I a) If the possibility of a faulty reading may be discarded, the small intervals in the increase in temperature are most probably due to an incapacity of the vessels to supply warm blood to such an extent as to permit an uninterrupted rise in temperature of the skin surface which is continuously loosing heat to the surrounding cool atmosphere. This incapacity might be secondary either to an arterial occlusion with well established collateral circulation as observed in the cases O 3, 11 and 6 (third examination) or to some remaining vasoconstrictor tone (S 15, 18, 29, 47, N 3, 9, 12). This phenomenon is, however, seen so often in the control subjects that no pathological significance is attributed to it. (Cf. Figure 2, page 39.)

I b) The variation seen between the variables that are all within the limits $3 \times$ S. D. if the fingers are counted as individuals is also probably due to a varying supply of blood to the fingers. This variation might be secondary either to an occlusion where the blood flowing to different fingers might have to pass unevenly developed collateral vessels before arriving at the fingers (O 1, 5) or variation in the constrictor tone of the fingers (S 3, 10, 15, 38, 46, 47, N 5, 6, 8, 12). This deviation was also so frequent among the controls that it was disregarded as indicating an abnormal state of circulation.

I c), I d), I e), I f), II b) have been discussed in the preceding paragraph.

II) The slow increase in temperature most probably is secondary to a diminished supply of blood to the finger. The supply of blood is large enough to convey some more heat than is lost to the surrounding cool air, but not large enough to permit a rapid increase in temperature. It is easily understood that this lack of supply might be secondary to arterial obstruction as well as prolonged moderate increase in vascular tone.

II a) The end temperature above 32° C measured after such an increase has the sole significance that it demonstrates a better supply of blood to that finger than to the finger with slow increase which does not attain such a temperature.

III) The failure to attain any obvious rise in temperature must be regarded as a sign of severe impairment of the finger blood circulation especially to the capacity of dilating after a vasoconstriction induced by cooling. It might be secondary to arterial occlusion as well as increase in vascular tone. It was supposed that the addition of ulnar nerve block or reactive hyperaemia could possibly distinguish between these two causes. As a matter of fact no case of occlusive vascular disease, where this incapacity was observed, revealed any rapid rise in temperature or tolerable end temperature after the addition of these complements to the examination. The patient with the local nerve injury (N 6) that did not demonstrate reactive hyperaemia after temporary arterial occlusion still rests obscure.

Summary

A material of various vascular disorders is investigated with the method described, and the results compared to those of the control material. The possibility to detect a person with impairment of the circulation of his fingers seems to be almost complete and the possibility to detect which fingers that have their circulation impaired rather good. There are no signs that definitely distinguish impairment secondary to occlusive vascular disease from that caused by increase in vascular tone, so-called functional or vasospastic disease. There are, however, some signs that are rather characteristic of either of these causes which might contribute to the differential diagnostics. If the method is completed by ulnar nerve block and/or reactive hyperaemia the possibilities to form an exact diagnosis are increased. It is emphasized that all fingers should be examined simultaneously.

CHAPTER V

PATIENTS WITH DIABETES MELLITUS

A. Introduction

Before insulin was introduced in the treatment of diabetes mellitus the general conception was that diabetic vascular disease was almost identical with arteriosclerotic disease. Some capillary disease also was considered to exist because many diabetics have a rosy colour on their cheeks (rubeosis diabetica) and also frequently capillary fragility. The diabetes of the young people, as a rule, was fatal before any arteriosclerotic disease had developed, but in elderly diabetics the progress of arteriosclerosis was known to be accelerated as compared with the common arteriosclerotic disease. The complications nephro- and retinopathy were regarded as inflammatory in origin without connection with any vascular disease in proper sense, and neuropathy as a degenerative lesion that could possibly be secondary to arteriosclerosis (v. Noorden 1907).

Since insulin has been introduced in the therapy, the life of the diabetic patient has successively increased, especially of the young diabetics. The predominant causes of death in diabetic disease have changed from coma and intercurrent infectious disease in the pre-insulin era to cardiovascular and renal disease (Joslin 1952).

There has been accumulating evidence that a general insufficiency in the most peripheral (terminal) circulation, i. e. arteriolar, capillary and venular circulation, might be the common cause of the diabetic complications, arteriosclerotic vascular disease, nephropathy and retinopathy (Dry & Hines 1941 Megibow & al. 1949, Broch & Kløvstad 1950, Handelsman, Levitt & Conrad 1952, Mendlowitz, Grossman & Alpert 1953, Lundbaeck 1953, Megibow & al. 1953, Bárány 1955). As regards the connections between diabetic neuropathy and terminal vascular disease the opinions have varied. Many authors, Broch & Kløvstad among others, consider diabetic neuropathy as being secondary to circulatory disturbances, but Martin (1953) is of the opinion that diabetic neuropathy is developing independent of vascular disease and may cause vascular symptoms through disturbances of vasomotor function. A survey of the problem of the neuropathy is given by Fagerberg (1956).

The natur of the terminal vascular damage still remains obscure. Many

observations, however, have been used as a basis for theories on the nature of the vascular dysfunction. Müller (1937) found a capillary dilatation in the skin of diabetics and considered this dilatation to cause a slow blood flow through the capillaries, followed by anoxaemia and vascular damage. Megibow & al. (1953) were of the opinion that a capillary damage with an increase in the resistance to blood flow caused the vascular disease. Ditzel (1954, 1956) and Ditzel & Sagild (1954) further have demonstrated changes of the corpuscular blood stream in the terminal conjunctival vessels of diabetic subjects which might cause reduction of the blood flow. Bárány (1955) concluded that the ultimate cause of the various vascular reactions of diabetes mellitus might be a lesion to the capillaries, but he had performed experiments which indicated a delayed inactivation of vasoconstrictor substances at the receptors in the vessel wall.

Ditzel (1956) observed by capillary microscopy on the conjunctival vessels of 220 diabetic and 175 control subjects that the diabetics had changes of all these types. The arterioles were constricted, the venules dilatated and especially in older patients hyaline infiltrations were observed in the walls of the terminal vessels.

There are thus very different opinions on the origin of the terminal vascular dysfunction in diabetes. Perhaps more concluding evidence could be gained by anatomical studies, but such studies of small vessels in diabetics have been almost entirely limited to the renal, retinal and conjunctival vessels. There is no information in the literature on anatomical studies as regards the small vessels in the fingers of diabetics.

The present clinical investigation on the reactions of the small vessels in the finger tips was completed with a study of diabetic patients. Studies on the terminal circulation of the legs in diabetics have been performed by Megibow & al. (1949), Handelsman & al. (1952), Mendlowitz & al. (1953), Megibow & al. (1953), Martin (1953) and Bárány (1955) and on small materials of other authors.

Megibow & al. (1949) investigated 48 patients with digital plethysmography. None of the patients had any signs or symptoms of vascular disease at clinical and arteriographic examinations. Twelwe of them reacted abnormally on tetraaethylammonium-injections.

Megibow & al. (1953) completed these studies with digital plethysmography on the big toes of 47 diabetics younger than 45 years. They showed no symptoms or signs of peripheral vascular disease in the extremities, as judged by ordinary clinical diagnostic methods including arteriography. Significant changes in blood flow were recorded after oral supply of nitroglycerine. Similar reactions could not be obtained in a control series of the same age distribution. They considered their observations to represent an occlusive vascular disease in the finer vessels of the toes. They proposed these vascular disorders to be

analogous to the lesions of diabetic retinopathy and renal intercapillary glomerulosclerosis. They also claimed that the increase in peripheral resistance to blood flow, which ought to accompany a terminal angiopathy could explain the increase in frequency and rapidity in development of arteriosclerosis in diabetics.

Handelsman & al. (1952) studied a series of 16 diabetics with a duration of disease from 10—15 years, also without symptoms or signs of vascular disease of the feet. They made similar observations as Megibow & al.

Mendlowitz & al. (1953) investigated calorimetrically the hallucal circulation of 38 young diabetics without symptoms or signs of vascular disease in the legs and found the heat dissipation of the big toe diminished in 9 of the diabetics as compared to the control material. There was a statistically significant difference between the heat dissipation of the diabetic and the control group.

Martin (1953) tested 5 control subjects, 5 recent diabetics without complications and 20 cases of diabetic neuropathy in the legs with skin thermometry on the thumbs and the big toes during body heating. He observed that neuropathy was combined with either an inability of the toes to be cooled to 18 —20° C or a low temperature of the toes at the beginning of the cooling which was not much further decreased. The thumbs always cooled during air cooling. When body heating was applied through a radiant heat-cradle, the cooled toes failed to rise in temperature. After an intravenous injection of 50 mg Priscoline there was an increase in temperature of the toes to at least 30° C within 30 minutes. All reactions were normal in the thumbs. On the basis of his observations Martin believes that not only damage to the autonomic vasomotor fibres occurs in all cases of neuropathy, but that also vasodilator and vasoconstrictor fibres to the skin of hands and feet exist separately.

Bárány (1955) investigated the heat dissipation from the skin of the feet and calves of 150 young male diabetics without signs of vascular disease in the legs and 83 male controls of corresponding age. The heat dissipation from the diabetics during body heating by radiant cradle was found statistically lower than from the controls. The difference between the controls and diabetics was increased the more the heating was prolonged. If a tibial nerve block was added during heating, the heat dissipation attained the same magnitude in both groups.

No investigations have been published on the finger circulation in diabetics except Martin's which did not really refer to the study of finger blood flow. Neither symptoms nor signs of impaired circulation in the fingers are described in connection with diabetes. This fact does not exclude the possibility of subclinical impairment of the finger circulation in the diabetic disease.

The angiopathy in diabetes is assumed to be generally distributed in the body (Lundbaeck 1953). If this hypothesis is correct the vessels in the fingers

ought to be involved. The impairment of the finger circulation might be recorded with a method sensitive enough. The present method was considered to be applicable in this respect.

One advantage of performing the investigation on the fingers instead of the toes would be a diminished influence of arteriosclerosis on the examination results, as arteriosclerosis is generally less pronounced in the arms than in the legs (Hevelke 1956). The frequency of arteriosclerosis in diabetics is high and the onset of arteriosclerosis comes early in life, but this fact cannot be regarded as a proof of the diabetic angiopathy being synonymous with arteriosclerosis. In order to elucidate the diabetic angiopathy the author considered the study of the circulation of the arms preferable to that of the legs.

B. Material

The diabetic material originally consisted of 99 patients. Seven of these were, however, excluded from the series because of coexisting symptoms and signs of disease which might influence the results of the temperature examinations. These symptoms and signs were:

1. Attacks of pallor and numbness in the fingers,
2. Degenerated cervical disc with paresis of one arm,
3. Chronic polyarthritis and psoriasis,
4. Hypertension, that was treated with hexamethonium.

One more case was excluded because of occlusive arteriosclerotic disease of the legs that was manifested three months after the temperature examination.

The remaining material contained 91 diabetic patients: 43 females and 48 males, varying in age between 14 and 70 years (Table IX). None of them had any history of vascular disease from the hands. Nor were there any signs of circulatory impairment in the hands as judged from inspection, pulse palpation or oscillometry of the wrists. There were no signs of cardiac insufficiency.

The patency of the circulation of the legs was also tested by inspection, pulse palpation and oscillometry. Most of the diabetics complained of cold feet, but with a few exceptions there were no signs of impaired blood flow by clinical examination. In one case (D 56) one of the posterior tibial pulses was missing. The oscillometric indices were yet normal on his ankles. Another case (D 95) had an oscillometric index somewhat low in one ankle, 0.5 scale units. He also had a scar on this ankle. He had, however, rather high oscillometric indices at his calves and no other signs of vascular disease but for calcification of the arterial media at roentgen examination. This sign is not considered being of much importance in the genesis of arteriosclerotic ischaemia (Dible 1956). Finally one patient had double-sided clubfoot (D 42) and had

no pulses palpable at the ankles and no oscillometric deflections. His leg arteries demonstrated extensive calcification of the media. The two patients last mentioned (D 42, 95), however, had normal temperature reactions except in one finger each and for that reason they were included.

Six patients had had oedema of the ankles some weeks prior to the temperature examination (D 35, 43, 60, 78, 96, 99). At the time of investigation one of them had manifest oedema. In four of these patients (D 35, 43, 60, 96) there was no increase in finger temperature when heating the feet, but the two others reacted normally in most fingers. As a matter of fact these two patients had had oedema closer to the examination than the others. Another patient (D 90) had no oedema at the first examination, but manifest oedema of the ankles at a repeated examination one year later on. Her fingers reacted normally at both examinations.

It has already been quoted from the literature that the circulation of the legs of diabetic patients might be impaired in rather many cases where other signs or symptoms of vascular disease are not observed (Chapter V A). This faulty circulation could possibly interfere with the results of the present investigation. For that reason the procedure used in the present investigation in some cases was combined with a later examination of the skin temperatures on the toes in the manner of Brattgård & al. (1952). There were 8 patients in this group, without increase in temperature in feet during the hot bath, that demonstrated normal temperature curves of the fingers, though this increase in temperature was induced by heating the apparently abnormal feet. This material will be published by Fagerberg (1957).

The patients were otherwise subjected to the routine clinical and laboratory examinations. There were two patients with the appearance of Cushing's disease (D 7, D 64), red, round face, »buffalo obesity», and striae on the abdomen and hips. They both had moderately elevated blood pressure and a rather benign diabetes where insulin therapy had not been instituted. Their temperature reactions were normal (D 7) or almost normal. Four of the male diabetics, who had contracted their illness in infancy were of rather short stature (D 20, 23, 35, 48), one of these was sexually immature (D 23) and another mentally backward (D 48). They all failed to reach the end temperature of 32° C except D 35, who had one temperature examination with prolonged periods of latency.

Four patients with advanced nephropathy had a moderate anaemia with 8.8—12.2 g haemoglobine/100 ml. (D 11, 23, 35, 97). They all revealed abnormal temperature examinations in one (D 11) or more fingers. The anaemia was considered as a part of their nephropathy and the possible influence on the examinations for that reason was neglected.

Other facts of interest in the disease, considered in the further description are recorded in the tables. These are arranged according to the duration of diabetic symptoms. The group of less than one year's duration has been

separated from the rest of the material because these patients had been victims to disease for a short time. The group of duration more than 16 years is about comparable to the »long term» diabetics of Lundbaeck (1953).

The control of the diabetes was exerted by the Medical Department of Länslasarettet of Mölndal in 49 of the 91 patients and by the Medical Clinic I of Sahlgrenska sjukhuset in Göteborg in the remaining 42. The patients in the first group were rural or suburban and the others urban. Since August 1952 the treatment of the two groups was approximately the same. Before this time no medical department existed at Mölndal and many of the patients of this group were treated by various doctors as a rule not specially trained in internal medicine. Some of these patients, however, also had been controlled by the internists at Sahlgrenska sjukhuset. In earlier periods of their disease some of the patients in the Göteborg group had also been treated by various physicians, with somewhat different opinions on the treatment of diabetes mellitus. Because of the varying management of the diabetics no attempt was made to compare the two groups.

The material is not representative of the diabetes in either Göteborg or the surrounding province. The material was selected to illustrate the incidence of abnormal vascular reactions in various stages of the disease. Furthermore cases of diabetic gangrene were excluded. The material may for that reason not be compared to those of Lundbaeck (1953), Aarseth (1953) or others, as regards the age and sex distribution of the patients, frequency of complications etc.

C. Results of Temperature Examinations

In most diabetics the hands could be cooled to about 15° C in the manner generally adopted. The only failures were registered in two patients with increased basal metabolic rate (D 7, 12). In two cases there were signs of neuropathy in the arms (D 35, 61) and they still did not reveal any diminished power to constrict their vessels. This is in contrast to the observations of Martin (1953).

The increase in temperature on heating the feet was quite normal in 24 cases, when only the first examination on every patient was considered (Table IX). Twelve patients showed only one or more fingers with pauses in the increase in temperature (I a) or some variable of the temperature curve normal in itself, but deviating statistically more than 3 × S. D. from the mean of the hand (I b). These minor aberrations were as usual not considered pathological.

Prolonged periods of latency appeared in 10 individuals on at least one examination. In the discussion on vascular disorders prolonged periods of latency are considered as a most probable indication of increase in vascular tone. Prolonged periods of latency were never observed in occlusive vascular disease (Chapter IV). For that reason some increase in vascular tone might

be part of the diabetic vascular disease. There was only one individual in the control material with this abnormality. A χ^2-calculation in the appearance of prolonged periods of latency in normals and diabetics demonstrated a slight significant difference ($0.02 > P > 0.01$). In three of these individuals, prolonged periods of latency were observed in some fingers simultaneously to failure to attain end temperatures above 32° C in others. The other abnormalities of the temperature curves with end temperatures above 32° C were (I e, I d, II a) registered in fingers of 10 individuals as the sole deviation, from the normal and in 7 in combination with other fingers failing to attain 32° C.

End temperatures below 32° C were observed in fingers of 36 patients. Seven of these patients had this abnormality only in one finger, two of whom with a duration of disease less than one year. Fifteen patients could not achieve the end temperature 32° C in any finger.

Reactive hyperaemia was induced in 9 patients of the 36 where 32° C was not obtained in some fingers. In 6 of these no further increase in temperature was registered (D 35, 47, 63, 83, 97, 100), in two there was a slight increase but no eligible end temperatures (D 20, 76) and only in one (D 95) was there a rather good increase in temperature in all fingers with end temperatures above 32° C in nine. In four of these experiments ulnar nerve block was applied simultaneously or sequently to the reactive hyperaemia. Three of these blocks were not followed by any further increase in temperature (D 63, 76, 83) but one (D 35) was accompanied by a rapid increase in temperature in the two left ulnar fingers. The temperature of 32° C was, however, not attained in these fingers either.

Four patients (D 20, 23, 47, 63), where further dilatation through reactive hyperaemia had been tried in three, were subjected to arteriography of one arm.[1]) No occlusions were seen and the contrast medium filled the arteries completely to the finger tips. In one case (D 47) there were isolated arteriosclerotic plaques distally in the ulnar artery with a slight constriction only. In another case (D 20) the arteries were rather narrow and seemed to be constricted, but without signs of intimal incrustations. The same picture of constricted arteries on arteriography was shown by the patient who had not been subjected to the reactive hyperaemia (D 23). The patients (D 20, 23 and 47) had acetylcholine 1/1000 slowly injected by the catheter into the brachial artery until pain was felt in the hand, and the skin of the arm had assumed a bright red colour. The arteriography was then repeated. The arteries of case D 20 had now dilated obviously and the passage of the contrast to the veins accelerated. In case D 23 the roentgen picture was not changed by the acetylcholine-injection. In case D 47 no further dilation of the arteries was observed but the passage of the contrast medium to the veins was accelerated.

[1]) The roentgen examinations were performed at the Roentgen Department of Länslasarettet, Mölndal.

The finger temperatures were measured during the acetylcholine-injections which were performed at a room temperature of 20—22° C. All the finger temperatures rose above 33° C after the injections.

Comments. The prolonged periods of latency in several cases, the rapid increase in temperature after reactive hyperaemia in the case D 95 and the radiographic appearance of the arteries in the case D 20 after the injection of acetylcholine support the opinion that increase in vascular tone participates in the forming of the diabetic vascular disorder. This increase in vascular tone is not always restricted to the terminal vessels according to the arteriographic pictures in case D 20.

The failures to attain end temperatures above 32° C could be caused by some obstruction to the blood flow. Probably this obstruction could not be situated in the subclavian, axillary or brachial arteries as the oscillometric readings and pulses were normal at the wrists. Nor were arterial occlusions probable in the arteries of the forearm because of the normal pulses in the wrists. The cases where arteriography was performed on the arm support this opinion, and also make the conception of arterial occlusions of the arteries of the hands rather unlikely. The slight constriction observed in the ulnar artery of case 47, could plausibly not induce any pathologic vascular reactions especially as the corresponding pulse was well palpable. If there were occluded vessels causing the failure to attain 32° C these vessels must be too minute to be visualized at arteriography. If there were complete obstructions in the minute vessels, extended enough to prevent increase in temperature in cooled fingers after heating the feet, there ought to be at least symptoms and also signs of impaired circulation in the fingers. As there were no such signs there were probably no occlusions. A permanent constriction of the vessels, however, might explain all these observations on patients with failure to attain the end temperature of 32° C.

An increase in vasoconstrictor tone was not likely to cause this failure to attain 32° C either, because this increase in tone ought to be relieved by an ulnar nerve block.

The observed dysfunction in the terminal vessels of diabetics was inhibited by the direct stimulation by acetylcholine, but not by the induction of reactive hyperaemia.

D. Results of Some Repeated Examinations

The temperature examinations were repeated on 22 cases during the course of the diabetic disease (Table IX).

The repeated examinations were accomplished with an interval of only a couple of days on two patients (D 44, 83). The results were not quite equal.

In both cases several fingers failed to reach the eligible end temperature of 32° C. Some fingers, however, reacted normally one day and pathologically another. If all the fingers were regarded as an entity the result was the same at both examinations.

Four of the patients (D 31, 49, 51, 90) demonstrated normal reactions at both examinations with intervals of 11 days to 10 months.

The remaining 16 patients may be classified into three groups according to the tendency to change the vascular reactions from the first examinations to those later on: 1) Cases with stand-still, 2) Cases with progress, and 3) Cases with regress of the vascular reactions.

1. Three patients (D 20, 47, 97) showed almost identical results at all examinations with intervals of 3—18 months. All their fingers failed to attain the temperature of 32° C after heating. All had been careless about therapy during the disease and did not change their habits between the examinations. They also had both nephro-, neuro- and retinopathy after 11—20 years of diabetes.

2. Five patients (D 16, 35, 36, 40, 63) had more marked abnormalities of the temperature curves at the second examination than at the first. The intervals were 1—7 months.

One of these patients (D 16) was in rather a bad state of control the whole time with persisting acidosis in spite of treatment. The increase in abnormality, however, was not very pronounced. At the first examination she had normal reactions, at the second one finger showed too small an increase in temperature (I e). The other two patients had had periods of one year or more of rather neglected treatment prior to the first examination, but were well adjusted after that time. The cases D 36 and D 40 changed their temperature reactions from normal to pathological but had end temperatures above 32° C. The patients D 35 and D 63 demonstrated a marked progress of their diabetic disease between the examinations and also showed more pronounced abnormalities of their vascular reactions. At the first examination there were still some normally reacting fingers but at the second and following examinations the increase in temperature was slow and no finger reached 32° C.

All patients in this group were above the mean of the diabetics in age. The patients D 35 and D 63 had had diabetes for 25 and 18 years respectively.

3. Eight patients, (D 5, 8, 27, 30, 32, 33, 38) demonstrated more or less pronounced decrease of the severity of the vascular reactions from one examination to another. They had all been rather careless about their diet as well as insulin before the first examination, but more careful between the examinations. Their disease had lasted from 2—21 years.

In case D 5 all fingers reacted pathologically after two years of diabetes with neglected treatment. There were prolonged periods of latency in 9 fingers with normal end temperatures but the right thumb showed only a slow increase and did not reach 32° C. After two years of strict control of the diabetes all fingers reacted normally.

Case D 8 had especially neglected the diet until the first temperature examination 10 years after the onset of disease. She then had five fingers with moderately abnormal reaction, but normal

end temperatures on all fingers. During the following year she was more careful but yet often acidotic. At a second examination, six months after the first, three fingers reacted abnormally and the reaction was perhaps more pronounced than before as two of them did not attain the eligible end temperature. Another 18 months passed and she was still more rigorous about treatment, but the tendency to show acidosis was persistent. At a repeated examination all fingers, however, were normal in temperature reactions.

Case D 9 had a known duration of diabetes of 10 years before the first examination. She had refused insulin but had no complications. After the first examination she still refused insulin but tried to follow the dietary restrictions. At the first examination there was only a slow increase in temperature and no normal end temperatures. At the second the increase in temperature was still slow, but all end temperatures exceeded 32° C.

Case D 27 demonstrated two fingers with slow increase in temperature, but normal end temperatures after 8 years of careless treatment. A year later with a more restricted life she had normal reactions in all fingers.

Case D 30 had a diabetes duration of two years before the first examination. He then revealed only two fingers with rapid increase in temperature, and two other fingers with slow increase were the only ones to exceed 32° C. Seven months later with a careful regimen all fingers except three were normal and these three fingers attained 32° C after a slow increase in temperature.

Case D 32 had had diabetes for 12 years at the first examination. She had taken insulin regularly but neglected diet. Two examinaitons with an interval of three months did not show any signs of vasodilatation after heating. She was persuaded to undertake also dietary restrictions and a year later four fingers on the left hand showed normal or almost normal reactions. The fingers of the right hand still failed to attain the end temperature 32° C. All but one of them had a slow increase in temperature.

The cases D 33 and D 38 were brother and sister with a duration of diabetes of 17 and 21 years respectively. Both had been extremely careless about diabetic therapy, insulin as well as diet, for long periods. At the first examination failure to attain 32° C as end temperature was revealed in 6 and 10 fingers respectively. About a year later when they had been rigorous in diet, even become vegetarians, they demonstrated normal (D 33) and one single abnormal finger (D 38) at the control examination.

Comments. The results of the examinations with only some days interval demonstrate that the temperature examinations in diabetics are not constant. If the examinations were estimated according to the most impaired finger the result was constant, however.

In seven patients the same results of the temperature examinations were observed from time to time.

In no case a diabetic with normal temperature reaction at the first examination lost the ability to attain the end temperatures above 32° C at the second one. In a couple of cases, however, a normal reaction became moderately abnormal in spite of a rather good regulation of the diabetes. In another couple of cases a moderately abnormal temperature reaction became severely abnormal during deteroriation of the disease.

In some cases, finally, a more rigorous control of the disease was accompanied by the appearance of more normal vascular reactions.

The results of these repeated examinations, thus, demonstrated that the vascular dysfunction in diabetics, recorded by the present method, was reversible and probably favourably influenced by a strict combination of dietary restrictions and adequate insulin therapy.

E. Discussion

The temperature reactions on fingers of diabetic patients may have the same origin as the vascular reactions on the legs studied by other authors. This origin still remains obscure. There are three main theories:

1. Degenerative lesions of the vessel wall.
2. Changes in the vasoconstrictor tone of the vessels.
3. Disorders of the local humoral regulation of the vessels.

1. Degenerative lesions of the vessel walls causing the diabetic angiopathy were advocated by Megibow & al. (1949, 1953) as regards the skin, and by numerous other authors considering the eyes and kidneys (Warren & Le Compte 1952, Thiel 1956). The vessel damage was considered as arteriosclerotic by Dry & Hines (1941) inter alia, but in recent years the hyaline infiltrations, demonstrated in the minute vessels in diabetic vascular disease of the kidneys, were supposed to originate from polysaccharides of the blood (Mc Manus 1949). The evidence cumulating in favour of this opinion caused Törnblom (1956) to administer DDD (2.2-bis parachlorophenyl—1.1-dichloroethane) in order to depress the serum polysaccharide level with promising results.

In the present investigation there were several observations favouring the assumption of infiltrations to the vessel walls also in the finger vessels. In case the heating of the legs was not enough to relieve the constrictor tone reactive hyperaemia was also performed. This mode of dilatation should have effected an increase in circulation had the vessel walls been sufficiently elastic. In the cases of vascular disorders the reactive hyperaemia always could produce a dilatation provided that there was no damage to the walls of the vessels as in the cases of occlusion or sclerodermia.

An ulnar nerve block could not induce any further increase in temperature either, when performed after 35 minutes of heating the feet. A dilatation should have occurred after the nerve block, an increase in constrictor tone being the cause of the failure to dilate on heating.

These two observations, e. g. the reactions on reactive hyperaemia and nerve block, imply some stiffness of the vessel walls, that could be secondary to infiltrations.

2. There is general agreement upon the vasometer tone of the skin of the hands and feet being regulated only by vasoconstrictor nerves (Folkow 1955,

Gaskell 1956). This is especially the case with the arteriovenous anastomoses of the digital ends (Folkow 1955). Martin (1953) in his experiments on diabetic neuropathy observed several patients in whom the skin temperature of the feet could not be depressed at a room temperature of 18° C. On the other hand he could not increase the temperature in cooled neuropathic feet, where peripheral dilatation was elicited by a heat cradle on the trunk. Histamine did not provoke flares at the skin of the legs in any of his patients. He drew the conclusion that there was damage to the autonomic vasomotor fibres in all the cases of diabetic neuropathy. This is probably true. Shapiro & Stoner (1955) observed vasodilatation to be permanent for months after peripheral nerve injuries. Odel, Roth & Keating (1955) observed similar loss of vasoconstrictor tone at diabetic neuropathy. No failure to induce vasoconstriction in legs with diabetic neuropathy has, however, been observed at this laboratory according to the method of Brattgård et al (1951). The failure to induce vasoconstriction observed by Martin might be due to his use of air for cooling. This is no reliable medium to cool the skin of the hands as demonstrated in this investigation. The feet should certainly react with vasoconstriction to a slightly higher temperature than the hands (Sheard & Horton 1939) but the room temperature used by Martin was also higher than the one used for this investigation. It was also demonstrated in the present work that a high BMR might influence the results of cooling. The incidence of patients who cannot be cooled in the neuropathy-material of Martin, however, is significant as compared to his control subjects and the diabetics without neuropathy.

Another observation of Martin that cooled feet could be re-warmed by heating the trunk is in line with the findings in the present work. In the same way Martin's experiences with priscoline injections, causing increase in temperature where indirect heating had failed, is in line with the observations with acetylcholine in my investigation. His interpretation of the results indicating the separate existence of vasodilator and vasoconstrictor fibres is, however, hazardous. The failure to induce vasoconstriction by cooling might, no doubt, be secondary to a degeneration of the vasoconstrictor fibres. The failure to induce vasodilatation, however, could have the same origin (Chapter IV). This effect could only be studied by the addition of a nerve block, which was not done. The dilatating effect of priscoline is mainly effected directly on the vessel walls (Mendlowitz 1954).

As regards the results of the present investigation the prolonged periods of latency are probably secondary to an increase in vascular tone (Chapter IV H). The other abnormalities of the temperature curves may also be caused by an increase in vascular tone, even the failures to reach the end temperature of 32° C. The ulnar nerve blocks, which were unable to induce vasodilatation, where the heating had failed in this respect, is an argument against the

increase in vascular tone being the sole cause of the abnormal vascular reactions observed in diabetics.

The observations of Ditzel (1956) on the conjunctival vessels indicate that both nervous influence and alterations of the walls of the terminal vessels participate in the formation of the diabetic angiopathy. Preferably in young diabetics he observed arteriolar constriction and venular distension. In older persons there were more often hyaline infiltrations in the walls of the terminal vessels. Assuming that the vascular alterations of the fingers were similar to those of the conjunctiva, the present observation of the prolonged periods of latency will correspond to arteriolar constriction and the failure to attain a sufficiently high end temperature to hyaline infiltrations.

3. Bárány (1955) advocates the presence of a disturbed humoral regulation of the vessels with diabetic angiopathy on the following basis. The heat dissipation, he observed from the calves and the soles of the feet of diabetics, was successively decreased the longer the period of heating required to induce »heat reaction» and perspiration which were considered to indicate marked vasodilatation. The »heat reaction» was not defined, but may be interpreted as the patient feeling hot or looking hot.

Kuno (1956), however, stated that perspiration may appear before any increase of heat elimination from the body is actually required because of the heat accumulation in the body. Hellon & Lind (1956) investigated the blood flow in one forearm and the simultaneous perspiration from the skin of the other. Three out of 11 subjects demonstrated continuous increase in blood flow after onset of perspiration, three a transient increase, three a decrease, and three unchanged blood flow. The variation of blood flow in the arm after onset of perspiration was therefore considered to occur at random.

In my material the control subjects and the normally reacting diabetics perspired on the forehead and the trunk at about the same time as the temperatures of the fingers passed 30° C. The sensation of heat was experienced at about the time when the period of rapid rise in temperature commenced i. e. 2—10 min. earlier. The diabetics with pathological temperature curves of the fingers frequently experienced sensation of heat and perspired for a long time before there was any increase in temperature of the fingers. Sometimes sensation of heat and perspiration occurred without increase in finger-temperature. For reasons mentioned »heat reaction» and perspiration appear doubtful as indicators on the stage of dilatation in the skin vessels of the extremities.

The decreasing regression line observed by Bárány on correlating the heating time used to the heat dissipation in diabetics might thus be due to his criteria of complete vasodilatation. Bárány may have recorded the heat dissipation in the limbs before their vasodilatation was completed. The decreasing regression line observed by Bárány is for that reason no definite

proof of a humoral regulation of the terminal blood flow. The arguments presented here, however, do not exclude this possibility.

The success of acetylcholine in provoking an increase in temperature, when injected intraarterially, could be interpreted as an argument against the presence of infiltrations in the vessel walls. As observed from the arteriographs, of the diabetics there was a general dilatation of the arteries supplying blood to the terminal vessels. Much of this blood was evidently returned to the veins very fast and thus the precooling effect of the vein blood (Vanggaard 1941, 1943, Bazett & al. 1948) should be diminished, especially as these investigations were performed in rather warm laboratories. After acetylcholine injection, the blood arriving at the periphery ought to be almost of body temperature. The arterioles would not need any pronounced dilatation to allow a high skin temperature. The capillaries, no doubt, were dilated according to the high colour of the skin. Yet, in two cases (D 23, 47) the temperature of the skin was not higher than about 33° C. It is not improbable that normally functioning terminal vessels of the skin would have permitted the skin temperatures to reach 35—36° C, especially as the room temperature was well above 20° C.

The conclusions of this discussion are:

1. The temperature reactions of the fingers indicate the vascular dysfunction of the finger ends of diabetic patients being either functional or organic or both.

2. In case they are functional there is an increase in the vasoconstrictor tone.

3. In case they are organic the vessels are constricted and rigid but not occluded.

4. The possibility of a humoral mechanism causing the change of the blood flow in the diabetic finger tips cannot be excluded.

The results of the repeated examinations do not add any information, facilitating the settlement of this problem.

Summary

A material of 91 diabetic patients without symptoms of vascular impairment of the arms is studied by using the method of reflex vasodilatation described. Signs of vascular impairment are revealed in 53 of the patients. This vascular impairment is considered to be due partly to an increase in vasoconstrictor tone, partly to some infiltration of the walls of the minute vessels. A humoral regulation is not regarded as necessary to explain the experimental results, but cannot be excluded. The vascular impairment is observed to be reversible after a careful treatment of the diabetes.

CHAPTER VI

RELATIONSHIP OF THE VASCULAR REACTIONS IN PATIENTS WITH DIABETES MELLITUS

A. Relationship to Different Parameters of the Diabetic Patients

The relations of the vascular reactions observed in the present investigation to other characteristics of the diabetic patients such as age, sex, duration, age at onset, insulin, acidosis, control etc. were studied. For this purpose the patients were classified in three groups on the same principles that were used for those with vascular disorders in a limited sense; furthermore according to the finger with the most impaired vascular reaction. Only the first examination was calculated where repeated examinations had been performed. To recapitulate the classification:

1. *Normal temperature reactions* (N) were considered to be present when all fingers showed temperature curves within the limits $3 \times$ S. D. or when the deviations I a or I b outside the limits were present.

2. *Moderate pathological temperature reactions* (M) included all other patients where all fingers attained the eligible end temperature of 32° C (I c, d, e, II a), and

3. *Severely pathological temperature reactions* (S) the patients that failed in this respect (I f, II b, III).

The statistical method used was χ^2-analysis.

1. Relation to Age, Sex and Duration of Disease

The material was divided into three groups according to age. It consisted of rather young patients probably because cases of gangrene or manifest vascular symptoms of the legs were not included. There was no significant correlation between the age of the patients and the frequency and severity of the vascular reactions ($0.2 > P > 0.1$). (Figure 4.)

The frequency of arteriosclerosis seems to be equal in male and female cases (Le Compte 1955). The male patients in the series demonstrated more severe reactions than the female, but this preponderance was not significant, either the whole material was considered ($0.1 > P > 0.05$) or the group with less than one year's duration was excluded ($0.3 > P > 0.2$). (Figure 4.)

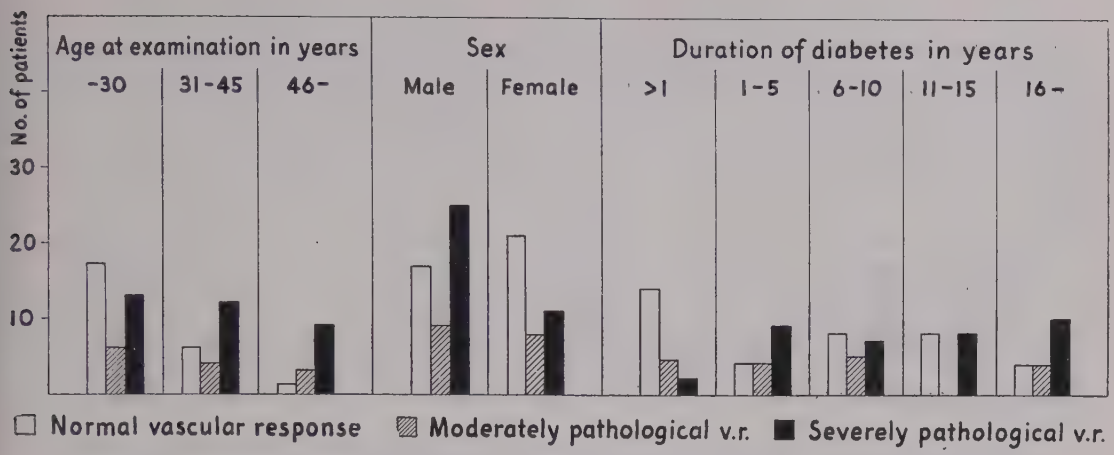


Figure 4. Correlation between vascular impairment and age, sex, and duration of disease of the diabetic patients.

In the present material the duration was correlated to the degree of vascular reaction with a slight significance ($0.05 > P > 0.02$) if the whole material was considered, but this correlation vanished if the group of less than one year's duration was excluded from the calculation ($0.3 > P > 0.2$). The frequency of pathological vascular reactions in the group with less than one year's duration was significantly different to the same frequency in the other groups ($0.001 > P$). (Figure 4.)

2. Relation to Age at Onset of Diabetes

Joslin (1952) showed that the incidence of onset of diabetes is about the same from the first to the eighth decade of life. Dahlberg & al. (1947) observed a preponderance of contracting diabetes in higher ages with a maximum between 50 and 60 years of age. The present material was, however, sampled in order to get comparable groups of the same duration. There was consequently a deviation of the material towards a higher frequency in the groups of lower age at onset. According to Joslin »Diabetics developing the disease at the age of 60 exhibit it generally in a mild form like that of the fat diabetic between 40 and 60, but as the period advances the type of diabetes reverts to that of youth in many instances». Bárány (1955) observed a correlation between heat dissipation of the calves and feet and age at onset of diabetes, but this correlation was essentially due to the covariance between the age at onset and the duration of the diabetic process. Lundbaek (1953) could not either find any correlation between diabetic manifestations and age at the onset. Ditzel (1956) observed, however, changes in the terminal retinal vessels that were correlated in distribution to the age at the onset of disease.

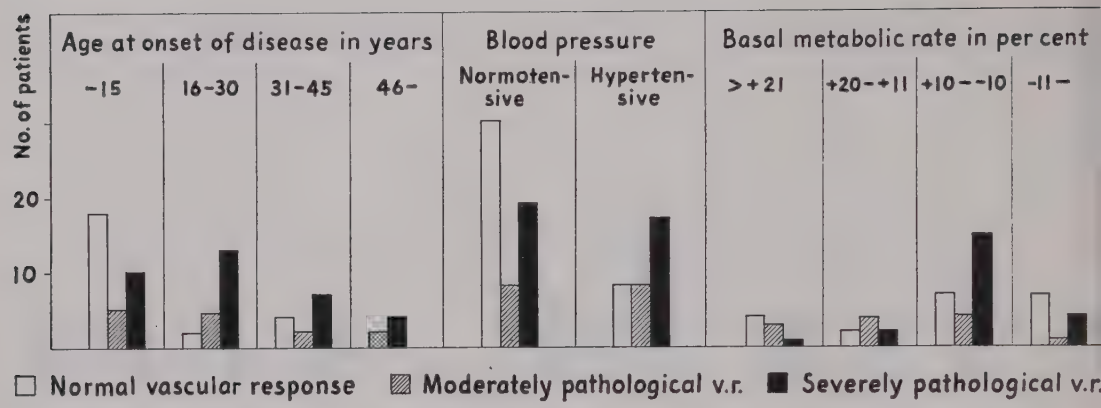


Figure 5. Correlation between vascular impairment and age at onset of disease, blood pressure, and basal metabolic rate of the diabetic patients. In the diagrams of age at onset and basal metabolic rate, the patients with a duration of less than one year are excluded.

In the present material there was no significant correlation between the duration of the disease and the number of individuals with pathological temperature reactions on the fingers in the groups with more than one year's duration. The group of less than one year's duration deviated from the rest of the material and was for that reason excluded from this calculation. The remaining material was divided into three groups with ages at onset under 15 years, between 16 and 45 and above 46 years. If these groups were compared as regards the the incidence of abnormal vascular reactions there was a slight significant correlation ($0.05 > P > 0.02$). Moreover, the dispersion of the material according to duration and age at the onset showed that long duration was correlated to low age at the onset ($0.01 > P > 0.001$). Thus the diabetics in this material had greater inclination to show a pathologic vascular reaction in the fingers with increasing age at the onset. (Figure 5.)

3. Relation to Blood Pressure

Root (1952) considers hypertension to be a sequela rather than a cause of diabetes. Hypertension is thought to provoke capillary sclerosis (Moschcowitz 1949). The frequency of hypertension in a material will depend on the limits set for the normal blood pressure (Aarseth 1953). These limits are drawn in different ways by various authors. The definitions of Skouby (1956) have been adapted to the present series i. e. hypertension implies a systolic blood pressure exceeding 150 mm Hg or a diastolic greater than 100 mm Hg. These values are in accordance with Warburg (1943) but somewhat higher than those stated by Page & Corcoran (1946), and Mårtensson (1950).

All measurements of blood pressure in the present work were performed on

recumbent patients at rest. Many of the observations were, however, made on out-patients in the consulting room where generally somewhat greater pressure values are found than in the ward (Warburg 1943). The method of Riva-Rocci used is as a rule satisfying, but can sometimes be inexact in comparison to intraarterial blood pressure determinations (Engstedt, Holmgren & Ström, 1956 and Carlsten 1957).

With the limits stated there were 57 patients with normal blood pressure and 33 with hypertension in the material. The occurrence of hypertension was correlated to the presence of abnormal vascular reactions. No correlation was found, whether or not the group with less than one year's duration was included ($0.05 > P > 0.02$ equal). (Figure 5.)

4. Relation to Basal Metabolic Rate

According to Duncan (1951) thyrotoxicosis aggravates diabetes. Myxoedema is considered to be a rare complication of diabetes and not known to exert much influence on the diabetic state (Root 1952). Skouby (1956) did not find any difference between the patient with goiter and other patients of his diabetic series as regards the incidence of »late diabetic lesions».

It has previously been demonstrated in the present work that hyper- and hypothyrosis has a marked influence on the temperature reactions in the fingers (Chapter IV).

There were 10 patients in the diabetic series which had had a BMR above +21 per cent. Two of them showed slight signs of thyrotoxic disease (D 7, 12). Their fingers could generally be cooled to about 15° C in 20 minutes, but this temperature could not be obtained at one experiment on each of them. None of the ten patients had need of more therapy than sedation. D 12 had been subjected to subtotal thyroidectomy 4 years prior to the temperature examination.

In no case there was clinically manifest myxoedema.

The material was classified in 4 groups according to the BMR, above +21 per cent, +11 to +20, +10 to −10, and below −11 per cent (there were only three cases below −21 per cent). The correlation was calculated with the group of less than one year's duration excluded. No significant correlation was observed ($0.10 > P > 0.05$). (Figure 5.)

5. Relation to Hypoglycaemia

Insulin was thought to cause an increase in adrenaline production through the hypoglycaemia (Carmon, Mc Iver & Bliss 1924, Ernestene & Altschule 1931). The increase in blood adrenaline was considered to cause vascular constriction.

Raab (1953) concludes that »a specific pharmacodynamic action of insulin per se on the cardiovascular system has not been definitely proved».

Abramson & al. (1939) demonstrated plethysmographically that the forearm blood flow was significantly increased at 6 out of 11 experiments on 7 patients 1—2 hours after 40—280 I. U. insulin subcutaneously. In two experiments there was only a slight increase, in one no change and in two experiments a slight decrease of the blood flow. The skin temperature of the nailfolds increased at all experiments. The investigation was performed on schizophreniacs.

Lovett-Doust & Salna (1956) observed the skin circulation of two healthy men by skin temperature and stroboscopic examinations of the capillary circulation in the nailfolds. When insulin coma was induced, the capillary circulation and skin temperature decreased. An abruption of the coma with glucose was followed by an increase of these quantities. When Figure 1 in their paper was studied it was, however, evident that during the effect of insulin, before the hypoglycaemic reaction arose, there was an increase in the finger circulation in one subject, and a slight decrease in the other.

In my opinion the evidence presented speaks in favour of the concept that the therapeutic doses of insulin have no influence on the terminal circulation, with the possibility that a slight increase or decrease of blood flow may happen. The effect of hypoglycaemic reactions on peripheral blood flow is not yet settled.

Eight patients had not been treated with insulin of the present series of 71 patients with a duration of more than one year. Their duration of disease was 3—15 years. Three of them had a severe pathological temperature reaction, two a moderate and two a normal reaction. Three of these patients had incipient complications, one nephro- and two neuropathy. All these coincided with the severe pathological temperature reactions.

Twenty-one of the patients with insulin therapy had had insulin reactions of varying severity. No correlation was observed between the art of vascular reaction and the incidence of insulin reactions ($0.3 > P > 0.2$). This is in accordance with Skouby (1956) who could not find any correlation between the occurrence of insulin reactions and the presence of nephropathy or retinopathy.

The distribution of pathological vascular reactions on patients with or without protamine in their insulin was also calculated and no correlation observed ($0.5 > P > 0.3$). (Figure 6.)

6. Relation to the Control of Disease

The role of the control in preventing the appearance of complications to the diabetic disease has been subjected to divergent opinions.

Mirsky (1946) considered some form of vascular disease inevitable in every diabetic who lived long enough. Dolger (1947) neither observed any influence

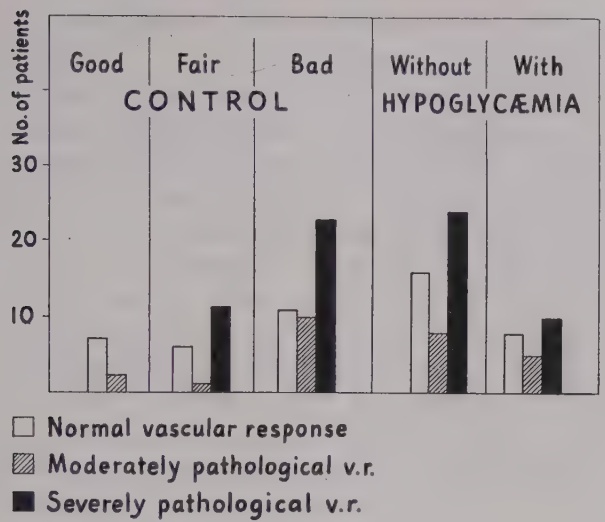


Figure 6. Correlation between vascular impairment and the incidence of hypoglycaemia and the control of the diabetic patients. The cases with a duration less than one year are excluded.

of the instituted therapy on the frequency of complications. He regarded the vascular damage as a part of the disease and not as a complication. This opinion has been shared by many investigators, in Sweden by Larsson, Lichtenstein & Ploman (1952) and Möllerström (1955).

Joslin and his co-workers (1952) have always maintained that careful regulation of blood- and urine-sugar through regulation of diet and insulin therapy may prevent the vascular lesions. They have considered the nephro- and retinopathy as real complications and not as inevitable elements of diabetes. Odin (1939), Engel (1950), Englesson (1954), Root, Pote & Frehner (1954). Andersson (1955), Krarup (1955), Matthews (1955), Skouby (1956) and Hagedorn (1957) share their opinion.

Lundbaeck (1953) divided his material in good and bad controls and observed a significant correlation between retinopathy and bad control, but no such correlation in case of vascular syndrome of the feet.

The present material was divided into three groups according to the control of the disease.

1. *Good* (G). The patient had followed the dietary and insulin prescriptions since the time when diabetes was diagnosed, which ought to have occurred within one month of the onset of symptoms. He had never been in coma and only occasionally had short periods of acidosis, thirst or polyuria. Blood sugar was regularly below 200 mg per 100 ml and urine sugar below 20 g a day.

2. *Fair* (F). The patient as a rule had followed the prescriptions. There had never been coma except at the onset of disease and symptoms of acidosis

were only occasional and slight. Blood and urine sugar were as a rule below 200 mg per 100 ml respectively 20 g a day.

3. *Bad* (B). All other cases. This group contained patients where acidosis and high blood or urine sugar had not been prevented in spite of all trials to regulate the metabolic disorder with dietary and insulin prescriptions. Most of the patients in this group had, however, neglected the prescriptions and control examinations during prolonged periods.

I have not attempted to evaluate the manner of treating diabetes used by various internists. The control was not estimated on the basis of complications from eyes, kidneys or nervous system. The classification was performed separately by me and another internist (Welin), and the differences in estimation discussed to a final conclusion.

The classification may be compared to the gradation used by Root, Pote & Frehner (1954) with the exceptions that no patient with excellent control is included and none of the diabetics performed daily controls of their urine at home. If the groups of good and fair control were conjoined, a group comparable to Lundbaecks fair control would be constituted.

There were only 9 patients with good control, 18 with fair and 44 with bad considering the diabetics with more than one year's duration. When the distribution of patients with various vascular reactions in these groups was calculated, a significant correlation was found ($0.01 > P > 0.001$). Good control thus implied a more normal vascular reaction (Figure 6). If the groups good and fair were conjoined and the calculation repeated there was no significant correlation ($0.2 > P > 0.1$).

The 29 careless patients were separated from the group and compared to the other patients with bad control regarding the vascular reactions. The patients who admitted carelessness did not differ from the others ($0.5 > P > 0.3$).

7. Discussion

The vascular reaction studied in this work is thus correlated to the age of the patients at the onset of diabetes in the material, but not to their duration of disease if this surpasses one year. This observation is contrary to the correlation between duration of diabetes and increase in frequency of complications observed by Engleson (1954), Skouby (1956) and others. Kramer & Perilstein (1955), however, accounted for a material of 3,000 diabetics where the complications were not correlated to the duration.

Ditzel (1956) demonstrated lesions in the bulbar conjunctiva of diabetic patients. These lesions were either characteristic of diabetes or of normal ageing. *The diabetic type of lesion was frequent in the diabetics with an early onset and the senile type in the others.* The typical diabetic lesions were arteriolar constriction, venular distension, irregularities of the walls of the terminal

vessels and perivascular oedema. The senile type of lesion consisted of hyaline perivascular infiltration.

Assuming that similar lesions cause the pathological vascular reactions of the fingers, the correlation to the age at the onset is more easy to comprehend. The increased tendency to arteriolar constriction in the young might explain the moderate pathological vascular reactions especially the prolonged periods of latency which have been considered as a sign of increase in vascular constrictor tone. This tendency to constriction should be reversible which might account for the decrease of pathological vascular reactions observed in some of the diabetics. The perivascular hyaline infiltrations in the more aged patients might cause an increased rigidity in the vascular walls, so that an inhibition of vasoconstrictor tone could not result in a vascular dilatation within a proper time. These hyaline infiltrations might also cause a complete loss of power to dilate. No complete loss of dilatation was observed in the hands when provoked by acetylcholine, injected intraarterially. The hyaline infiltrations might, however, be one cause of the diabetic gangrene, which, however, was not observed in the hands.

The relation of vascular reaction to control of diabetes seemed to be dependent on the patients of good control. The patients of fair control cannot be distinctly separated from those with bad control as regards the distribution of vascular reaction. The results of the repeated examinations emphasize this observation. Patients who were ambitious to follow the prescriptions were the sole to demonstrate improvement of their vascular reaction. The lack of correlation between the frequency of complications and control reported by several authors (Chapter V A) might be due to their insufficient demands on the control.

The absence of correlation of vascular reactions to age, sex, acidosis, insuline reactions, BMR and blood pressure contradict these factors statistically influencing on the other correlations established.

B. Relationship to other Complications of Diabetes

The augmenting incidence of the complications nephropathy, neuropathy and retinopathy to diabetes after the introduction of insulin in therapy has been regarded by Mirsky (1946), Dolger (1947) and others as a part of the disease that is due to appear in every diabetic patient who lives long enough. Joslin and his co-workers (1952), Lundbaeck (1953), Engleson (1954) and Skouby (1956) have brought forward evidence indicating that these signs are really complications that may be delayed and even avoided with a thoroughly accomplished therapy.

Regarding the connections between these three types of complications and their connection to arteriosclerosis there are also divided opinions. The opinion that all these four complications are secondary to a generalized disorder in the terminal (arteriolar, capillary and venular) circulation has been advocated by Lundbaeck (1953). Root & Kenny (1952) and Root, Pote & Frehner (1954) have used the collection term »triopathy» if nephro-, neuro- and retinopathy are coincident. Martin (1953) has regarded neuropathy as a degenerative lesion of the peripheral nerve fibres perhaps causing the vascular disease, but not secondary to it.

1. Relation to Nephropathy

Diabetic nephropathy was considered to occur if the patient had persistent proteinuria. Thus neither transient proteinuria accompanying acidosis nor occasional traces of protein in the urine were judged as caused by diabetic nephropathy. Most of the nephropathic patients had marked signs as proteinuria of 1 or more g/litre, pathologic urine sediment with red blood corpuscles and cylinders, and impaired renal function as judged from specific weights or clearance determinations.

No attempt was performed to divide this group according to the severity of the complication. Nor was it ventured to determine in what frequency chronic pyelonephritis might be the cause of the nephropathy as the urine sediment counts had been performed by different persons at different hospitals and bacterial cultures had not routinely been grown.

As previously stated 6 of the patients had had oedema of the legs prior to the temperature examination. The total number of nephropathic patients was 31 all with a duration of more than one year. The group of shorter duration was excluded from the following calculations as regards the age at the onset and the control.

The statistical calculations demonstrate a highly significant correlation between long duration and incidence of nephropathy ($0.001 > P$). Age at the onset of diabetes and control did not present any correlation to nephropathy ($0.8 > P > 0.7$ and $0.5 > P > 0.3$ respectively). The correlation between nephropathy and the pathological vascular reactions was highly significant ($0.001 > P$). (Figure 7.)

This correlation probably cannot be secondary to some other correlation previously found, as the duration is not correlated to the vascular reactions only to the incidence of nephropathy. The age at the onset and the control were only correlated to the vascular reactions.

If those patients were excluded from the calculations, who had had oedema of their legs, which might possibly interfere with the results, the significance of the correlation was diminished but still slight ($0.02 > P > 0.01$).

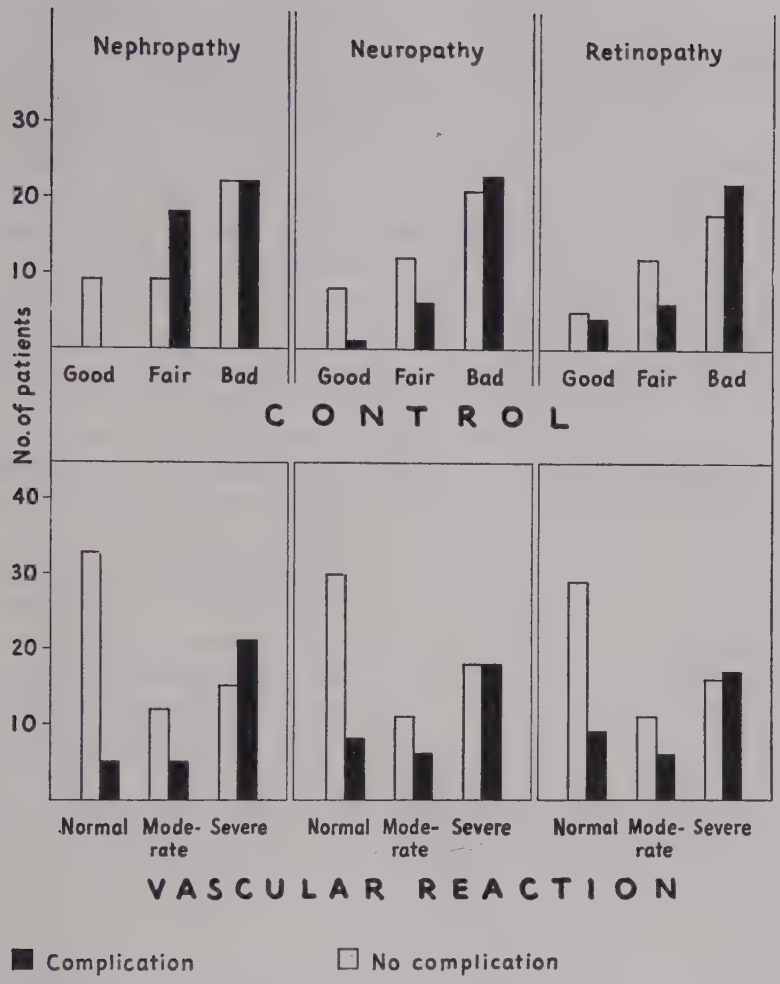


Figure 7. Correlation of the complications of the diabetic disease to the control of the disease, and to the incidence of vascular impairment.

2. Relation to Neuropathy

Neuropathy was defined to occur either if the Achilles tendon reflexes were absent — or almost absent — on both sides or the vibration sensibility was markedly impaired on one or both feet. A unilateral, weak Achilles tendon reflex might be secondary to a forgotten attack of sciatica. Two patients (D 15, 59) demonstrated diminshed reflexes only. They were, however, accepted as neuropathic cases having other symptoms indicating this diagnosis, i. e. absent patellar reflexes or impotence. Most of the neuropathy-patients had more pronounced symptoms and signs. The loss of vibration sense could be extended to the whole legs, and in two patients also to the forearms (D 35,

61). Impotence was admitted in some further cases (D 79, 83) and also diarrhoea (D 15, 43, 48). Most of the neuropathic patients complained of cold, numb feet and legs but none had real pain, and no paresis was observed. It was not resolved if these symptoms were secondary to the neuropathy or an angiopathy.

Two years prior to the examination pernicious anemia had been detected in one patient (D 47). The neuropathy in this case might be secondary to that disease, but the disease was diagnosed before much anemia had occurred. The anemia was corrected in a couple of weeks and was well controlled afterwards. The neurological disorder was revealed about the time of the first temperature examination. The diabetic disease and not the anemia has, therefore, been considered as a cause of the neuropathy.

There were two cases of neuropathy in the group of duration less than one year (D 36, 79). Both these patients were rather old, 55 and 58 years. They had perhaps contracted their disease earlier than was stated by their histories. The temperature reactions in their fingers were normal at the first examination. In case D 79 alcoholism might have caused the neuropathy.

The patients with neuropathy in the arms demonstrated a moderately impaired vascular reaction at the first examination. There was no difficulty observed at cooling their hands to 15° C within 10 minutes. Case D 35 was re-examined several times and then always demonstrated severe impairment.

Although including two patients with neuropathy, the group of less than one year's duration was excluded from the correlation to duration and age at the onset. No attempt was made to subdivide this group according to the severity of neurologic symptoms.

The incidence of neuropathy in the material was correlated to the duration and the age at the onset of diabetes with a slight significance ($0.05 > P > 0.02$ in both calculations). There was no significant correlation observed to the order of control ($0.10 > P > 0.05$). The correlation to the occurrence of pathological vascular reaction was also revealed as slightly significant ($0.05 > P > 0.02$). (Figure 7.)

In the correlation of neuropathy to the temperature reactions of the fingers the fact that both are related to the age at the onset of the disease may influence the calculations. Duration or control of diabetes may not exert any influence of this type.

3. Relation to Retinopathy

All patients except one (D 4) were examined by experienced ophtalmologists.[1]) Case D 4 revealed no signs of retinopathy at direct ophtalmoscopy

[1]) The ophtalmological examinations were performed either at the Ophtalmological Clinic of Sahlgrenska sjukhuset or by Dr. L. Öberg.

by the internist, but was yet excluded from the calculations. In three cases (D 43, 48, 61) catharact of both eyes prevented the inspection of the ocular fundi. These cases were also excluded from the calculations. The remaining series of 87 patients contained 33 cases of retinopathy. In one more case (D 42) there were slight signs of retinopathy in the shape of small blood streaks but this patient was hypertensive and lacked microaneurysm. Hypertension was the most plausible origin to his retinopathy according to the ophtalmologist. No attempt was ventured to subdivide the group by the severity of the retinal damage.

The incidence of retinopathy revealed highly significant correlation to the long duration of disease ($0.001 > P$). On the contrary there was no correlation to the age at the onset ($0.5 > P > 0.3$) and no correlation to the control of disease ($0.9 > P > 0.8$). As regards the occurrence of pathological vascular reactions there was a slight significant correlation observed ($0.05 > P > 0.02$). (Figure 7.)

No case of retinopathy was observed in the group of short duration that was not included in the calculations on correlation to control and age at the onset.

The correlation between the incidences of retinopathy and pathological vascular reaction might be influenced by the correlation of both retinopathy and vascular reaction to duration. When the group with short duration of diabetes is excluded, there still exists a correlation between retinopathy and duration, but none between vascular reaction and duration. There is no correlation retinopathy to age at the onset or control to duration of diabetes. For reasons mentioned the correlation between retinopathy and vascular reaction is considered to be real.

4. Discussion

Lundbaeck (1953) states, »the common denominator of the phenomena which we include in the designation long term diabetic syndrome is a vascular disease». In that syndrome he included the arteriosclerotic diseases of diabetics, either in the leg or the heart, the retinopathy and the nephropathy. The connection between the diabetic neuropathy and vascular dysfunction was less pronounced. Kornerup (1955) and Skouby (1956) observed correlations between proteinuria and retinopathy. Skouby could not find any reliable connection between the incidence of neuropathy and of other complications of diabetes. Martin (1953), as mentioned before, considered the neuropathy possibly causing the vascular disorder but not being caused by it.

In the present investigation the correlations of nephropathy and retinopathy to the vascular reactions of the finger tips are significant and probably

not disturbed by other factors with a common influence. For that reason it is natural to consider *the present results as another support to the unitary vascular origin of these two complications.* The relation of the vascular reactions to diabetic neuropathy is less significant. The present results cannot give any certain contribution to the solving of this problem. It must, however, be kept in mind that the vascular reactions in my work were investigated on the fingers, and the symptoms and signs of neuropathy were observed in other parts of the body than the arms except in two patients. These two patients only demonstrated a moderately impaired vascular reaction, i. e. they reached the eligible end temperatures above 32° C on all fingers, and their hands were cooled without difficulty. If a nerve degeneration had elicited the vascular reaction, there ought to have been a difficulty in cooling the hands and the increase in temperature, on heating the feet, should have been less pronounced (Martin 1953, Simeone & Felder 1951).

Summary

The correlation of the vascular reactions to various parameters of the diabetics and the complications of the disease was investigated. The occurrence of vascular impairment is correlated to the medical control of the patient with a high significance, and to the age at onset with a slight significance. The vascular impairment is also correlated to the presence of nephropathy with a high significance and to retinopathy with a slight significance. *This observation is interpreted as a sign of these three complications being parts of the same vascular syndrome.* There was no reliable connection between vascular impairment and the presence of neuropathy.

GENERAL SUMMARY AND CONCLUSIONS

Chapter I. The advantages and disadvantages of reflex dilatation and skin temperature measurements are discussed in comparison to other methods used for evaluating the digital circulation. My method of examination is described and the influences of various conditions of the experiment and the subject investigated and discussed. It is especially emphasized that an initial cooling of the digits to 15° C is essential, the room temperature ought to be below 20° C, and the heating bath temperature between 42 and 44° C.

Chapter II. A control material of 68 healthy people of varying sex and age is rendered. The influence of age, sex, time of the day, time of the year, and state of digestion on the method is accounted for and found negligible. The influence of smoking is not found to be significant, but the occurrence of individuals, sensitive to tobacco, must be considered. The stipulations for the courses of finger temperature curves during the present procedure to be accepted as normal are given and the conceivable deviations from the normal courses of temperature curves described. The signification of the various phases of the temperature curves are discussed.

Chapter III. A material of patients suffering from disturbed metabolic rate was examined with the method described. It was observed that the fingers of hyperthyrotic patients were difficult to cool but easy to re-warm. Hypothyrotic patients were normally cooled but were difficult to re-warm. This state of condition is reversible on adequate therapy concerning hyperthyrosis but not always concerning hypothyrosis especially of prolonged duration.

Chapter IV. A group of patients with various vascular disorders was investigated. The method affords supplementary information about the functional state of circulation of the digits that sometimes cannot be deduced by other methods of investigation. Especially in combination with ulnar nerve block and/or reactive hyperaemia the method can add to the accuracy of differentiating between vascular disturbances secondary to occlusions or increase in vasoconstrictor tone. A dependable separation between the two causes of vascular impairment may not be achieved. A good agreement was disclosed between the severity of vascular complaints and the finger temperature reactions. The signification of the phases in the temperature curves are further discussed on regarding the information collected from the material of vascular disorders.

Chapter V. The method was applied on a material of diabetic patients without symptoms or other signs of vascular disorders of the hands. Signs of vascular

dysfunction in the fingers were recorded with the present method on 53 out of 91 patients. The nature of the diabetic vascular disease is discussed. The results of the investigation as well as the reports of other authors are considered most compatible with the assuming of increase in vascular tone and infiltrations in the walls of the small vessels co-operating to create the picture of diabetic vascular dysfunction. A rigorous observance of dietary and therapeutic prescriptions seems to permit a recurrence of normal vascular function.

Chapter VI. The abnormal vascular reactions were correlated to various parameters of the diabetic patients. Correlation is observed to the age at onset but not to the age, sex, blood pressure, basal metabolic rate, or insulin reactions. The reaction was low in frequency only in diabetics of less than one year's duration, but was about equally dispersed in groups of longer duration. There is a significant correlation between the good control of the diabetes and the absence of pathological vascular reaction.

The relation of the diabetic vascular dysfunction in the digits to other complications of the diabetes was calculated. Significant positive correlations were observed regarding nephropathy and retinopathy and not significant as regards neuropathy. This correlation is regarded as a support of the opinion of the vascular dysfunction of the fingers, the nephropathy and the retinopathy being different manifestations of the same generalized vascular disease. The connection of the diabetic neuropathy to this vascular syndrome cannot be decided upon with the present results.

The applicability of the method. The method of studying the blood circulation in the fingers by reflex dilatation, the progress of which is controlled through finger temperature measurements, is in my opinion adequate in distinguishing normal from pathological vascular reactions. It gives a qualitative orientation on the state of circulation in the fingers and indicates disturbances of the peripheral circulation in patients who are not yet aware of their circulatory impairment.

The lack of ability to give quantitative values of the blood flow has no signification as regards the control of reflex vasodilatation. Reflex vasodilatation, however, is no method suitable for analyzing the *blood flow* in the finger tips. The rapidly varying temperatures on the skin surface will perhaps disturb the volumetric and calorimetric methods so that their measuring values will be doubtful (Chapter I).

It is often desirable to control the finger blood flow during some other procedure of investigation. It is then, as a rule, inconvenient to induce a reflex dilatation. Skin temperatures may be misleading if they are not measured during an increase in blood flow, preferably rapid. During such circumstances some of the methods, plethysmography, calorimetry or pulse volume determinations must be used. These methods cannot be applied to more than 1—4 fingers without advanced technical equipment.

For reasons mentioned the principal advantages of the present method are:

1. To select patients suitable for more advanced vascular studies.
2. To select fingers with impaired circulation and to determine on which finger the methods with limited application should be used.
3. To detect vascular dysfunction where circulatory abnormalities may be suspected but neither symptoms nor signs are present at the clinical routine examination (as in cases of diabetes).
4. To give an aid in the differential diagnostics of established peripheral vascular disorders, preferably with the addition of ulnar nerve block or reactive hyperaemia.

Simplification of the method. In this investigation the skin temperature measurements have been performed in order to establish the basis for skin temperature measurements on reflex vasodilatation. The method of proceeding with one measurement on each finger every minute, however, is somewhat exercising for the examiner and gives little spare time for adjustments on the experimental conditions. The examiner must be quick of apprehension. To permit a more widespread use of the method I have considered some simplifications eligible.

As I am still emphasizing the importance of examining all ten fingers at the same time the simplifications will concern the frequency of the measurements. It is no problem to perform one series of measurements and register them within one minute, it is the re-measurements each minute which are trying. To avoid too great discrepancy in time between the values measured they should be read within one minute for a series of fingers. The remaining possibility to facilitate the method is to increase the interval between the series of measurements.

An increase of the interval between the onset of the measurement series to 5 minutes will have no influence on the determination of the end temperature. The determination of the period of latency will neither be disturbed. If there are no signs of rapid increase in temperature within 30 minutes the period of latency is pathologically long and the time to consider addition of other methods of vasodilatation has arrived. According to the present method a normal finger circulation presupposes the presence of a rapid phase of increase in temperature where the increase of more than 1° C/min. must continue for more than 7.5° C, but less than 10 minutes. The problem is to capture this rapid rise with intervals between the series of measurements of 5 minutes. The values of 7.5° C and 10 minutes, however, are the widest limits permitted (3 × S. D.). A check of the control material demonstrates that only 6 fingers of 680 distributed in three subjects have an increase in temperature between the limits 2 × S. D. (= 10° C) and 3 × S. D. and that no finger has a period of rapid rise exceeding 9 minutes, which is the value of the limit 2 × S. D. To demand these, values of time and temperature do not increase the stipula-

tions of the method much. One of the periods of 5 minutes should then contain an increase of 5° C or more. If this increase is more than 7.5° C it can at once be accepted as normal. If the increase is less than 7.5° C, the sum of increases in temperature in the period before and after the period mentioned must exceed 5° C and most of the increase appears during one of these periods. With this procedure there will be some addition to the approximation of the method but there are always the possibilities of performing more frequent temperature determinations during some phase of the experiment and to repeat the experiment when doubtful. When the method is performed in this manner the number of temperature determinations in each examination will be reduced to 20 per cent or less of the number used in the related examinations.

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APPENDIX

TABLE I. *Result of Statistical Calculations.* The large squares contain the results of the total material. The small squares at the right side of the columns contain the results grouped according to sex. The small squares below the large ones contain the results grouped according to age. In the upper row the cause of grouping is placed in the left upper corner of the squares. The number of subjects in each group is given in the corresponding right corner. This information is not repeated in the other rows.

	Period of latency in minutes			Period of rapid rise in minutes			Increase in temperature in °C			End temperature in °C		
Means and Standard Deviations for a single finger, irrespective of the values of the other fingers.	Total 68 10.82 ±6.01		♂ 35 10.45 ±6.16 ♀ 33 11.23 ±5.82	Total 68 5.34 ±1.52		♂ 35 5.31 ±1.38 ♀ 33 5.37 ±1.66	Total 68 15.38 ±2.50		♂ 35 15.46 ±2.46 ♀ 33 15.30 ±2.54	Total 68 34.37 ±0.80		♂ 35 34.36 ±0.76 ♀ 33 34.39 ±0.82
	< 30 37 10.31 ±6.56	31—45 19 11.0 ±4.78	46—60 12 12.16 ±5.58	< 30 37 5.23 ±1.37	31—45 19 5.66 ±1.66	46—60 12 5.18 ±1.81	< 30 37 15.85 ±2.07	31—45 19 15.13 ±2.91	46—60 12 14.34 ±2.55	< 30 37 34.49 ±0.80	31—45 19 34.32 ±0.80	46—60 12 34.10 ±0.73
Standard Deviations for a finger calculated from the mean for all the fingers of the hand.	±1.41		±1.46 ±1.29	±1.04		±1.01 ±1.07	±1.43		±1.50 ±1.36	±0.51		±0.54 ±0.47
	±1.21	±1.47	±1.52	±1.52	±0.99	±1.12	±1.42	±1.38	±1.54	±0.49	±0.51	±0.55
Means and Standard Deviations for a hand irrespective of the value of the other hand.	10.82 ±5.89		10.45 ±6.03 11.23 ±5.72	5.34 ±1.21		5.31 ±1.05 5.37 ±1.36	15.38 ±2.12		15.46 ±1.95 15.30 ±2.23	34.37 ±0.66		34.36 ±0.61 34.39 ±0.71
	10.31 ±6.48	11.0 ±4.62	12.15 ±5.57	5.23 ±1.05	5.66 ±1.19	5.18 ±1.54	15.85 ±1.62	15.13 ±2.20	14.34 ±2.15	34.49 ±0.66	34.32 ±0.65	34.10 ±0.54
Standard Deviations for the hands.	±2.22		±2.13 ±2.32	±0.91		±0.81 ±1.00	±1.21		±1.30 ±1.10	±0.58		±0.54 ±0.61
	±1.21	±2.90	±3.19	±0.75	±1.20	±0.85	±1.12	±1.15	±1.52	±0.52	±0.68	±0.56

TABLE II. *Calculation on the Greatest Difference between two Fingers.*

	Finger No.	Mean	Standard error of the mean	S. D.	Standard error of the S. D.
Value of the finger with the longest period of latency	III	11.5	±0.62	±5.09	±0.44
Value of the finger with the shortest period of latency	IV	10.1	±0.69	±5.66	±0.49
Difference between these fingers		1.4			
Value of the finger with the longest period of rapid rise	I	5.8	±0.14	±1.61	±0.10
Value of the finger with the shortest period of rapid rise	V	5.0	±0.14	±1.59	±0.10
Difference between these fingers		0.8			
Value of the finger with the greatest increase in temperature	IV	16.1	±0.19	±2.23	±0.14
Value of the finger with the smallest increase in temperature	I	14.0	±0.21	±2.47	±0.15
Difference between these fingers		2.1			
Value of the finger with the highest end temperature	V	34.7	±0.06	±0.68	±0.04
Value of the finger with the lowest end temperature	I	33.8	±0.07	±0.79	±0.05
Difference between these fingers		0.9			

TABLE III. *Standard Deviations for the Differences between Repeated Examinations on Control Subjects.*

Differences calculated on:	Period of latency	Period of rapid rise	Increase in temperature	End temperature
Two almost identical examinations on 13 subjects	±3.75	±1.19	±1.69	±0.41
Two examinations on 7 subjects before and after onset of menstruation	±5.95	±1.54	±2.27	±0.57
Two examinations on 7 subjects in the morning, fasting and after lunch	±3.68	±1.86	±1.80	±0.91
Two examinations on 10 subjects at room temperatures of 15 and 18 °C	±5.35	±1.66	±2.48	±0.98
Two examinations on 8 subjects at room temperatures of 15 and 20 °C	±3.98	±1.44	±2.08	±0.62

TABLE IV. *Result of the Statistical Calculations.*

The limits of the variables calculated with a dispersion of 3 × S. D. permitted	Period of latency in minutes	Period of rapid rise in minutes	Increase in temperature °C	End temperature °C
The limit for the value of a finger irrespective of the values of the other fingers of the hand	***29**	**10**	**7.5**	**32**
The greatest permitted deviation for a single finger from the mean for the fingers of the hand	**5**	**4**	**4.5**	**2**
The limit for the mean value of a hand irrespective of the value of the other hand	**29**	**9**	**9**	**32**
The greatest permitted difference between the means of the hands	**7**	**3**	**4**	**2**
The limits of the variables calculated with a dispersion of 2 × S. D. permitted.				
The limit for the value of a finger irrespective of the values of the hand	23	9	10	32.5
The greatest permitted deviation for a single finger from the mean for the fingers of the hand	3	3	3	1.5
The limit for the mean value of a hand irrespective of the value of the other hand	23	8	11	33
The greatest permitted difference between the means of the hands	5	2	2.5	1.5

In this table the limits of the variables calculated with a dispersion 3 × S. D. and 2 × S. D. are given. The dispersion 3 × S. D. is printed in fat type since this dispersion has been considered as normal in the present work.

* As stated in text the limit of the period of latency was extended to 30 minutes when the pathological material was evaluted.

TABLE V. *Oral and Rectal Temperatures Measured Simultaneously to the Examinations on the Fingers. °C.*

No.	Oral temperature					Rectal temperature				
	Before cooling	After cooling	Onset of period of rapid rise	End of period of rapid rise	End of experiment	Before cooling	After cooling	Onset of period of rapid rise	End of period of rapid rise	End of experiment
16	35.9	36.4	36.3	36.0	35.8	36.8	36.6	36.4	36.4	36.3
27						37.0	36.8	36.6	36.5	36.6
27						36.6	36.8			36.6
28						37.2	36.9		36.9	36.8
45	35.8	37.1	37.3	37.4	37.4	37.2	37.4	37.3	37.4	37.4
48	36.2	37.0	37.2	37.3	37.0	37.0	37.2	37.3	37.3	37.3
51	36.9	37.6	37.6	37.6	37.5	37.5	37.7	37.8	37.7	37.6
67	35.6	36.8	37.5	37.6	37.6	37.2	37.4	37.5	37.6	37.6
S 15	36.0	37.3	37.7	37.8		37.2	37.5	37.6	37.7	37.9
D 20	37.1	37.8	*		36.3	37.6	37.8			37.8
D 20	36.5	37.1			37.4	36.9	37.0			37.6
D 35	37.1	37.3	37.2	37.6	37.6	37.0	37.2	37.2	37.4	37.6
D 47	36.6	36.6	36.6	36.9	36.9	37.4	37.2	37.0	37.1	37.1

* In case D 20 there is no rapid increase in temperature.

Key to the tables VI—IX. Abbreviations.

Series No.	The figures refer to the examination records.
Records No.	M. The Medical Department. Mölndal. M. M. The Out-patient clinic of this dpt. M. I. The Medical Clinic I. Göteborg. M. P. I. The Outpatient Clinic of M. I. N. K. The Neurosurgical Clinic. Göteborg N. The Neuromedical Clinic. Göteborg. K. I. The Surgical Clinic I. Göteborg. T. L. Private patients of Torsten Lindqvist M. D. Priv. Authors private patients.
Duration.	The figures refer to the symptoms of the disease. A question-mark denotes that the statement is uncertain.
Essential symptoms.	Ex. = examination. Persp. = perspiration. Recurr. = recurrence. d. = day. w. = week. m. = month. y. = year. Imp. = improvement A question-mark in the column Retinopathy denotes that a correct estimation is not possible because of catharact.
Blood pressure.	R = right. L = left. Question-mark = not measurable.
Oscillometric index.	The maximal oscillometer readings stand as numerators and the corresponding blood pressure readings as denominators.
Pulse palpation.	(+) denotes a pulse that is palpable but considerably weaker than the corresponding pulse of the other arm.

In the preceding colums only the results of the clinical examination at the first temperature examination are recorded. Results of later examinations are given only when an essential change has occurred.

Kind of insulin. (diabetes)	Di = one mixture of ordinary and zinc-insulin. NL = another mixture of ordinary and zinc-insulin. Ord = ordinary insulin. Z = zinc-protamin-insulin.
Control. (diabetes)	G = good control. F = fair control. B = bad control.

No. of fingers.	Path. reac. = pathological reaction. The deviations from the normal range I a and I b are not included in these figures as they are considered abnormal, but not definitely pathologic.
Fingers deviating from the normal range.	An underlined figure denotes that this finger showed symptoms the others not, or the symptoms and signs were more pronounced in this finger. A line in a vacant square has the same meaning. A = Amputated.
Character of finger symptoms (vascular diseases).	No = absence of vascular symptoms. Sl = slight vascular symptoms. Se = severe vascular symptoms.
Character of vascular reaction (diabetes).	N = normal vascular reaction. M = moderately impaired vascular reaction. S = severely impaired vascular reaction.
Reactive hyperaemia. Ulnar nerve block.	An increase in temperature to end temperatures above 32° C is denoted +, the others —. A (—) denotes that this experiment is not performed uniform to the others.

For further explanations see text.

TABLE VI.

Cases of Hyperthyrosis																			
Series No.	Record No.	Initials Sex Age	Clinical diagnosis	Duration in years	Essential symptoms and signs	Blood pressure syst./diast.	B M R	Serum cholesterol mg.100 ml.	Oscillometric index wrist		Pulse palpation wrist				No. of fingers with path. temp. reac.	Period of latency mean of 10 fingers	Period of rapid rise mean of 10 fingers	Increase in temp. mean of 10 fingers	
											right		left						
									right	left	rad.	uln.	rad.	uln.					
T 1	K. I. 4823/54	E. S. ♀ 30	Thyro-toxicos.	1	Nervous, hungry, warm, moist skin	145/75	+26	175	1.5/110	2/120	+	+	+	+	0	4.3	6.1	16.0	
T 2	K. I. 4745/54	G. J. ♀ 26	Thyro-toxicos.	1	Nervous, persp., tremor.	115/70	+30	195			+	+	+	+	0	5.9	3.9	16.0	
T 3	K. I. 4429/54	A. J. ♀ 40	Thyro-toxicos.	2/12	Nervous, tremor. Warm, moist skin.	150/85	+41	175	2.5/130	2/130	+	+	+	+	0	4.5	6.5	11.2	
T 4	K. I. 5712/54	I. M. L. ♀ 34	Thyro-toxicos.	6/12	Tachycardia, tremor, warm moist skin.	145/70	+66	140	2/140	2.5/150	+	+	+	+	0	2.6	3.9	13.9	
				1 1/12	Op. 8 m. after onset. Then cold.		+9	185							0	21.0	7.7	13.3	
T 5	M. 190514	A. E. ♂ 35	Thyro-toxicos.	1 6/12	Op. 6 m. after deb. Recurr. with persp. tachycardia	140/75	+85	173	2/120	2/130	+	+	+	+		Cannot be cooled below 25.5° C in 20 min.			
				1 11/12	^{131}I after ex. Slight impr.		+38									Cannot be cooled below 26° C in 20 min.			
T 7	K. I. 5936/54	N. S. ♂ 47	Thyro-toxicos.	1	Nervous, tachycard. Moist warm.	170/80	+55	140	3/160	3/170	+	+	+	+		Cannot be cooled below 19—23° C in 20 min.			
				1 2/12	Preop. treatment, not op.		+29								0	4.3	6.4	12.2	
T 8	K. I. 5079/54	E. H. ♀ 34	Thyro-toxicos.	1	Tachycardia, moist warm skin nervous. Op. 1 w. after ex. Improved condition. No hypothyreosis.	155/75	+54	145	4.5/120	5/130	+	+	+	+		Cannot be cooled below 21—27° C in 20 min.			
				1															
				1 4/12			+3	190							0	Cannot be cooled at all in cold air.			
T 9	K. I. 5052/54	K. J. ♀ 40	Thyro-toxicos.	6/12	Vasolabile, nervous, palpitation. Op. day after ex. Feeling cold.	135/60	+20	120	3/130	2.5/120	+	+	+	+	0	11.2	3.3	10.0	
				11/12			−10								2	24.3	6.4	11.6	Increase in temp. path. in thumbs.
T 10	M. I. 2874/54	G. J. ♂ 42	Thyro-toxicos.	3	Tachycardia, tremor, warm, moist skin.	155/90	+48	115			+	+	+	+		Cannot be cooled below 19—25° C in 20 min.			
T 11	M. 290204	D. J. ♀ 25	Thyro-toxicos.	3/12	Tachycardia, nervous, moist, warm. ^{131}I some days after ex. At 2nd ex. calm and not warm.	160/85	+52				+	+	+	+		Cannot be cooled below 25—27° C in 10 min.			
				5/12			+27								0	4.9	5.5	13.2	
				7/12			+6								0	10.0	4.4	16.6	
T 12	K. I. 4845/54	M. U. ♀ 46	Thyro-toxicos.	3/12	Tachycardia, nervous, tremor. Not op. before 2nd ex.	150/90	+64	150	3/110	2.5/110	+	+	+	+	0	3.1	5.5	10.9	
				4/12			+89								0	5.0	5.6	14.0	
T 13	K. I. 3705/54	A. B. ♀ 44	Thyro-toxicos.	7/12	Tachycardia, tremor, moist, warm skin. Op. 2 d. after ex. Improved.	140/90	+37	155	3/130	4/110	+	+	+	+		Cannot be cooled below 21—25° C in 20 min.			
				8/12			+14	216							0	11.7	6.4	12.9	
T 14	M. 121223	V. J. ♀ 42	Thyro-toxicos. Hypertens	2	Recurr. after ^{131}I. Tired.	190/110	+26	128	3/130	5.5/130	+	+	+	+	0	0.2	5.7	11.5	
T 15	M. 050826	G. H. ♀ 49	Thyro-toxicos.	6	Tired. Warm, moist skin.	120/80	+46	172			+	+	+	+	0	6.2	6.3	11.3	
T 16	K. I. 4487/54	C. S. ♀ 47	Thyro-toxicos.	5/12	Tachycardia, tremor, warm, moist skin. Exoftalmus. Op. one w. after ex.	150/65	+29	140	2/130	2/130	+	+	+	+	0	6.2	4.5	13.1	
				7/12			±0	350							0	20.8	6.1	14.0	
T 17	M. 080421	H. K. ♀ 46	Thyro-toxicos.	3/12	Tachycardia, tremor persp., nervous. ^{131}I 1 m. after ex. Cold tired.	160/70	+42		3/120	3.5/120	+	+	+	+		Cannot be cooled below 19—24° C in 20 min.			
				8/12		110/80	−24	390							0	10.4	6.3	12.7	
T 18	M. 210917	A. G.	Thyro-toxicos.	6/12	Tachycardia, nervous, tremor.	140/70	+34	195			+	+	+	+	0	6.9	6.0	18.0	

TABLE VII.

Cases of Hypothyrosis						Blood pressure syst./diast.	B M R	Serum cholestend mg/100 ml	Oscillometric index. wrist.		Pulse palpation wrist				No. of fingers with path. temp. reaction	Period of latency mean of 10 fingers	Period of rapid rise mean of 10 fingers	Increase in temp. mean of 10 fingers	End temp. mean of 10 fingers	Reactions deviating from the normal. No. of fingers.									Fingers deviating from the normal range. Distribution of reactions.									
											right		left							I						II		III	right hand					left hand				
Series No.	Record No.	Initials Sex Age	Clinical diagnosis	Duration in years	Essential symptomes and signs				right	left	rad.	uln.	rad.	uln.						a	b	c	d	e	f	a	b		1	2	3	4	5	1	2	3	4	5
M 1	M. 900916	H. O. ♂ 64	Myxoedema	20	Tired, dry skin, cold hands, mentally slow. More alert, skin not so dry at 2 nd ex. Angina pectoris provokes a decrease in thyroid therapy. Small progress of symptoms at 3rd ex.	120/90	−11	326	6/140	6/140	+	+	+	+	10	32.3	7.2	13.7	33.9			10								I c	I c	I c	I c	I c	I c	I c	I c	I c	I c
				20 3/12			± 0	169							5	11.0	5.8	8.0	33.6	5				4		1			II a	I a	I e	I e	I e	I e	I a	I a	I a	I a
																of nine fingers																					
				20 9/12			−23								1	8.7	7.0	11.3	33.1	6						1			II a	I a	I a	I a		I a			I a	I a
																of nine fingers																					
M 2	M. 970917	A. S. K. ♀ 57	Myxoedema	16	Tired, dry pale skin, thin hair and eyebrows Slight precordial pains increased during thyroid therapy.	200/110	−22	600	2.5/130	2.5/120	+	+	+	+	10				32.3			1		2		2	5		II b	II b	II b	II b	II b	I e	I e	II a	II a	I c
				16 3/12		180/120	−18	300							10				19.0								5	5	III	III	III	III	III	II b	II b	II b	II b	II b
																													10	III	III	III	III	III	III	III	III	III	III
M 3	M. 050221	E. M. ♀ 49	Myxoedema	8/12	Coarse dry skin, hoarse. White fingers in cold (not numb). Cardiac enlargement. Symptoms vanish gradually on thyroid therapy.	200/110	−19	435	2/150	2/150	+	+	+	+	10																								
							−11	263							10				30.5			2			3		5		II b	I f	I c	I c	II b	II b	II b	I f	I f	II b
				1 4/12											0	23.1	9.4	14.9	34.0																		
				1 9/12																																		
M 4	T. L. 242/54	S. T. ♀ 24	Myxoedema	8/12	Coarse dry skin. Cold.	120/90	−34		1.5	1.5	+		+		0	5.9	4.5	11.9	34.1																		
M 6	M. M. 001022	I. A. ♀ 54	Myxoedema	4	Tired, cold., coarse dry skin. Flat T-waves. Good condition, normal E C G after therapy.	170/110	−17		2/120	1.5/120	+	+	+	+	10				33.5							10			II a	II a	II a	II a	II a	II a	II a	II a	II a	II a
							+12								1	8.4	8.0	13.6	34.5	4			1						I d					I a		I a	I a	I a
				4 3/12																																		
M 7	M. M. 360530	B. Å. ♀ 18	Myxoedema	1	Cold, tired, dry skin. Improved by thyr. therapy, interrupted before 2nd ex.	110/80	−16		2/130	5/110	+	+	+	+	9				31.1						8		1		I f	I f		I f	I f	II b	I f	I f	I f	I f
							−17								2	9.8	5.2	8.7	32.9	1	2			2					I b					I b	I e		I a	I e
				2 6/12																																		
M 8	M. I. 3673/53	J. A. ♀ 59	Myxoedema	10	Thyroidectomized, dyspnoe tired.	165/90	−10	215			+		+		0	16.9	6.9	16.2	34.7		1								I b									
M 9	M. 130720	E. H. ♀ 42	Myxoedema	1/12	Thyrotoxicosis treated with ^{131}I resulting in hypothyreosis. »Corrected» again with thyr. ther.	130/90	−21				+	+	+	+	10				27.7						7		3		II b	II b	I f	I f	I f	II b	I f	I f	I f	I f
				1			−13								5	15.6	6.6	11.6	32.0	2					5				I f	I f	I f	I f	I f			I a		I a
M 12	M. 980911	A. G. ♀ 57	Myxoedema	15	Coarse dry skin, hoarse. Flat T-waves on E C G.	140/90	−22	525			+	+	+	+	7	35.5	9.2	13.9	33.4	2		5		2						I c	I e		I e	I c	I c	I c	I a	I c	I a
M 13	M. 291003	I. W. ♀ 27	Myxoedema	3/12	Tired, cold, dry coarse skin, palpitations.	130/90	−33	370	2.5/110	2.5/110	+	+	+	+	0	15.8	6.1	15.9	34.5																		

TABLE VIII.

Cases of vascular disorders: Series No.	Record No.	Intials Sex Age	Clinical diagnosis	Duration in years	Essential symptoms and signs	Blood pressure syst./diast.	B M R	Serum cholesterol mg/100 ml	Oscillometric index wrist: right	Oscillometric index wrist: left	Pulse pulpation wrist: right rad.	Pulse pulpation wrist: right uln.	Pulse pulpation wrist: left rad.	Pulse pulpation wrist: left uln.	No. of fingers: with symptoms	No. of fingers: with symptoms and path. reac.	No. of fingers: without symptoms with path. reac.	Reactions deviating from the normal No. of fingers: I a	I b	I c	I d	I e	I f	II a	II b	III	Fingers deviating from the normal range. Distribution of reactions: right hand 1	right hand 2	right hand 3	right hand 4	right hand 5	left hand 1	left hand 2	left hand 3	left hand 4	left hand 5	Character of finger symptoms	Reactive hyperaemia	Ulnar nerve block
1. Cases of arterial occlusion																																							
O 1	M. I. 2444/53	A. W. ♀ 37	Arteritis in right brachial artery	6	1950 both ulnar and radial arteries occluded. 1953 brachial artery occluded, ulnar recanalized. Cold right 3rd and 4th finger.	130/30			0	1.25/140	–	–	+	+	2	0	1		3					1			I b	A	I b	I b	II a						Sl		
				6											2	1	1		2				2				I b		I f	I b	I f								
				7 6/12											2	1	1					2								I e	I e								
O 3	M. 070622	I. D. ♀ 48	Arterit. brachiocephalicus	2	Constriction of both subclavian arteries and right brachiocephalic artery. Left hand cold.	R 160/90, L 120/110	188	1.5/90	0.8/70		+	–	(+)	–	5	2		1				1		1									II a	I a		I e	Sl		
O 5	T. L. 83/55	N. L. ♂ 44	Mb Buerger	4/12	Constriction of right radial artery. Right 1st and 2nd fingers cold. No symptoms at 3rd ex.	120/80	+21		3/100	3/100	–	+	+	+	2	2	0						1		1		I f	II b									Sl		
				6/12											2	0	0		2								I b	I b											
				1 2/12					4.5/100	4.5/100					0	0	0		2								I b	I b											
O 6	M. 970802	E. R. ♀ 58	Arterit. brachiocephalicus	20?	Constriction of both subclavian and left carotid arteries. No symptoms from fingers.	?	+1	300	0	0.2/70	–	–	–	–	0	0	10								10		II b	II b	II b	II b	II b	II b	II b	II b	II b	II b	No		
				20?											0	0	9						1	4	4		II a	II b	II b	II b	II b	II a	II a	II a		I f			(–)
				21?		R ?, L 105/90			0	0	–	–	–	–	0	0	1	4						1			II a		I a	I a	I a	I a							
O 8	M. I. 2835/52	M. B. ♀ 35	Arterit. brachiocephalicus	14	No symptoms from fingers. Aortography failed.	R 100/80	+36		1/110	1/110	(+)	(+)	+	+	0	0	0																				No		
				16		L 115/90	+17		2/80	2.5/90	(+)	(+)	+	+	0	0	2				1			1			II a	I d											
O 9	M. P. I. 7257/56	A. L. ♂ 37	Mb Buerger	2/12	Right radial artery constricted and tortuous, ulnar occluded. Cold fingers right hand.				2:0	2.5	(+)	–	+	+	5	5	0									5	III	III	III	III	III						Se	–	
				2/12											5	2	0	1	1					2			II a	II a		I b	I a								
				3/12					3.0	4.5					5	5	0								1	4	II b	III	III	III	III							–	
O 10	M. I. 1043/56	A. N. ♀ 76	Embolus in right brachial artery	1/12	Cold, cyanotic right hand, with pale fingers. No pains. Sensitivity for pinpricks normal.				0	1.5/100	–	–	+	+	5	5	0									5	III	III	III	III	III						Se	–	
O 11	M. I. 115/56	D. P. ♀ 39	Arterit. brachiocephalicus	21	Left subclavian artery occluded. No cold fingers	R 125/70, L 95/80		218	1.5/90	0.2/90	+	+	–	–	0	0	4	2			3	1					I e	I a		I a	I d	I d			I d		No		

(*Cont.*)

TABLE VIII. (*Cont.*)

Cases of vascular disorders: Series No.	Record No.	Initials Sex Age	Clinical diagnosis	Duration in years	Essential symptoms and signs	Blood pressure syst./diast.	B M R	Serum cholesterol mg/100 ml	Oscillometric index wrist		Pulse pulpation wrist				No. of fingers			Reactions deviating from the normal. No. of fingers.									Fingers deviating from the normal range. Distribution of reactions										Character of finger Symptoms	Reactive hyperæmia	Ulnar nerve block
									right	left	right rad.	right uln.	left rad.	left uln.	with symptoms	with symptoms and path. reac.	without symptoms with path. reac.	I a	I b	I c	I d	I e	I f	II a	II b	III	right hand 1	right hand 2	right hand 3	right hand 4	right hand 5	left hand 1	left hand 2	left hand 3	left hand 4	left hand 5			
2 a. Cases of »dead fingers»																																							
S 10	M. M. 240701	A. J. ♀ 30	Dead fingers	6/52	1946 hot swollen hands.	130/90	−9	203	1/100	1/100	+	+	+	+	10	0	0		2															I b		Ib	Sl		
S 12	M. 950906	B. J. ♀ 60	Dead fingers	2	Hands and feet cold between attacks.	135/90	−3		4.5/130	5/130	+	+	+	+	10	4	0						4				I f	I f	I f	I f							Sl		
S 24	Priv. 300626	L. S. ♂ 24	Dead fingers	17	Slight troubles only.				3.5/90	4/90	+	+	+	+	10	0	0																				Sl		
S 29	M. 380503	K. K. ♀ 17	Dead fingers	10?	Cyanotic oedematous feet. Slight troubles from hands.	140/80	−9	270	3.5/120	3.5/130	+	+	+	+	10	0	0																				Sl		
				10?											10	2	0	1			2						I d		I a			I d							
S 35	M. 220415	A. L. ♀ 35	Dead fingers Hemicrania	10/12		120/80	+12	261	2.5/100	3/100	+	+	+	+	10	0	0																				Sl		
S 41	M. P. I. 7524/56	S. K. ♀ 22	Dead fingers	5	Similar complaints of knees not feet.				1.5	1.5	+	+	+	+	10	0	0																				Sl		
S 46	Priv. 321121	B. L. ♀ 22	Dead fingers	7		125/90			2.5/110	2.5/110	+	−	+	−	10	0	0		2									I b					I b				Sl		
				7											10	0	0																						
2 b. Cases of Raynaud's disease																																							
S 1	T. L. 5/52	E. A. ♀ 44	Raynaud's disease	25?	Attacks also at room temp.	130/90	+17				+		+		10	10	0			5				3	2		I c	II a	II a	II a	II b	I c	I c	I c	II b	I c	Se		
S 2	T. L. 25/53	E. G. ♀ 46	Raynaud's disease	6	Frequent paronychial infections		+10	260			+		+		10	7	0		1	7								I c		I c	I c	I b	I c	I c	I c	I c	Se		
S 3	M. I. 3012/51	E. J. ♀ 45	Raynaud's disease	7	Attacks by distress. Scar on the right index.	120/60	+15				+		+		10	0	0		5								I b	I b	I b	I b	I b						Sl		
S 4	M. I. 777/51	G. G. ♀ 26	Raynaud's disease	6	Minor complaints recently	135/90			1.2/130	1.3/100	+	+	+	+	10	0	0																				No		
S 5	M. M. 160509	G. L. ♀ 38	Raynaud's disease	30?	Attacks also in warm water. Slight trouble from feet.	105/80	+4				+	+	+	+	10	0	0																				Sl		
S 8	T. L. 228/53	M. A. ♀ 54	Raynaud's disease	35?	Calcinosis in the skin of the digital ends.		−5		1.7	1.2	+	+	+	+	10	9	0			5				3	1		I c	II a	II b	II a	—	I c	I c	I c	I c	II a	Sl		
S 11	M. 110716	I. S. K. ♀ 43	Raynaud's disease	28?	Attacks from cold wind, not water.	120/80	+1		3/110	3/110	+	+	+	+	10	10	0			5			1		4		II b	I f	I c	I c	II b	II b	II b	I c	I c	I c	Se		
				29?											10	1	0								1		II b											+	
S 15	Priv. 310721	R. M. R. ♀ 24	Raynaud's disease	10	Attacks also from warm wind and water.	115/90			2/90	1.5/100	+	+	+	+	10	5	0	4			1		4					I f	I f	I f	I f	I a	I a	I d	I a	I a	Sl		

(*Cont.*)

TABLE VIII. (*Cont.*)

Series No.	Record No.	Initials Sex Age	Clinical diagnosis	Duration in years	Essential symptoms and signs	Blood pressure syst./diast.	B M R	Serum cholesterol mg/100 ml	Oscillometric index wrist: right	Oscillometric index wrist: left	Pulse pulpation wrist: right rad.	right uln.	left rad.	left uln.	No. of fingers: with symptoms	with symptoms and path. reac.	without symptoms with path. reac.	Reactions deviating from the normal. No. of fingers. I a	I b	I c	I d	I e	I f	II a	II b	III	Fingers deviating from the normal range. Distribution of reactions: right hand 1	2	3	4	5	left hand 1	2	3	4	5	Character of finger symptoms	Reactive hyperæmia	Ulnar nerve block
					Cases of vascular disorders																																		
S 16	M. M. 120913	E. J. ♀ 43	Raynaud's disease	5	Sometimes blue skin to middle of forearm.	125/90	— 2		3.5/100	2/100	+	+	+	+	10	0	0		2													I b	I b				Sl		
S 17	M. M. 180517	A. W. ♀ 37	Raynaud's disease	2	Attacks also in left foot.	140/100	—17	255	1.5/120	1.5/120	+	+	+	+	10	0	0																				Sl		
S 18	M. M. 171017	S. N. ♀ 38	Raynaud's disease	13	Attacks also at room temp.	140/90			3/100	2.5/100	+	+	+	+	10	0	0																				Sl		
S 21	T. L. 296/52	E. G. ♀ 37	Raynaud's disease	6	Scars on the right finger tips 2nd, 3rd, 4th.				1.5	1.5	+		+		10	8	0			6			1			1		I c	—	I c	I c	I c	I f	III	I c	I c	Se		
S 30	Priv. 301008	N. E. A. ♂ 25	Raynaud's disease	10 11	Attacks from cold wind in the morning, seldom water.	120/80			4.5/90	7.5/90	+	+	+	+	10 10	10 10	0 0						 3		 1	10 6	III III	III III	III I f	III I f	III I f	III III	III III	III III	III III	III II b	Se	 +	+
S 31	Priv. 180421	I. S. ♂ 37	Raynaud's disease	30?	Complaints also of feet.	125/80			2/100	2.5/100	+	+	+	+	10	9	0			6			1			2	I c	I f	III	I c	I c		III	I c	I c	I c	Sl		
S 32	Priv. 131205	M. J. ♀ 42	Raynaud's disease	25?		140/85			3/120	2.5/120	+	+	+	+	10	0	0																				Sl		
S 36	M. 100811	A. A. ♂ 46	Raynaud's disease	10	More trouble from left hand.	120/80	+ 6	173	1.5/120	1.5/120	+	+	+	+	10	7	0			2	1	1				3	I e		I d			III	III	III	I c	I c	Sl	+	
S 38	T. L. 20/56	H. S. ♂ 46	Raynaud's disease	2	Three right ulnar fingers have scars.		+ 2	240	4.5	4.5	+	+	+	+	10	3	0		1						3			II b	—	II b	II b			I b			Sl		
S 40	M. I. 582/56	A. L. E. ♀ 45	Raynaud's disease	20?		150/85	—11		5/120	3/120	+	+	+	+	10	10	0			10							I c	I c	I c	I c	I c	I c	I c	I c	I c	I c	Sl		
S 43	T. L. 68/56	N. Å. L. ♂ 44	Raynaud's disease Hemicrania	35?	Similar troubles of feet.	155/100	+ 1		4.5	5.5	+	+	+	+	10	10	0									10	III	III	III	III	III	III	III	III	III	III	Se	+	
S 47	M. I. 6959/54	T. J. ♂ 39	Raynaud's disease	7/12 7/12	Most complaints of right 3rd—4th fingers. Scar on 3rd.	130/80			4/90	4/90	+	+	+	+	10 10	3 1	0 0	 2	3 3			1 	 1	1 	1 		II a I a	I b I b	I b I b	II b I f	I b I b	I e I a					Sl		
					3. Cases of sclerodermia																																		
S 9	M. 901011	A. A. ♂ 66	Sclero-dermia	1 2 2	Trophic changes, all finger ends. Sclerodermia of face, elbows, oesophagus. Ulcer on left index after 2 y.	160/80			5.5/140	5/140	+	+	+	+	10 10	10 10	0 0								4 8	6 2 10	III II b III	III II b III	III II b III	III II b III	II b III III	II b II b III	III II b III	II b II b III	II b II b III	III III III	Se	 —	 —
S 25	N. K. 070116	B. R. ♀ 48	Sclero-dermia	10	Trophic changes, all finger ends. Sclerodermia, face, elbows, right knee.	130/80	— 1		2	2	+	+	+	+	10	10	0									10	III	III	III	III	III	III	III	III	III	III	Se		

(*Cont.*)

TABLE VIII. (*Cont.*)

Series No.	Record No.	Initials Sex Age	Clinical diagnosis	Duration in years	Essential symptoms and signs	Blood pressure syst./diast.	B M R	Serum cholesterol mg/100 ml	Oscillometric index wrist right	Oscillometric index wrist left	Pulse pulpation wrist right rad.	right uln.	left rad.	left uln.	No. of fingers with symptoms	with symptoms and path. reac.	without symptoms with path. reac.	Reactions deviating from the normal. No. of fingers. I a	I b	I c	I d	I e	I f	II a	II b	III	Fingers deviating from the normal range. Distribution of reactions right hand 1	right hand 2	right hand 3	right hand 4	right hand 5	left hand 1	left hand 2	left hand 3	left hand 4	left hand 5	Character of finger symptoms	Reactive hypræmia	Ulnar nerve block
S 26	N. 060128	Å. B. ♂ 49	Sclero-dermia	6	Trophic changes, 1st and 5th finger both sides. Similar complaints of toes.	140/90			4.4/140	3.5/140	+	+	+	+	10	10	0									10	III	III	III	III	III	III	III	III	III	III	Se		
S 37	M. 031220	A. O. ♂ 53	Sclero-dermia Diab. mell post cysta pancr. op.	15?	Scars on all fingers except thumbs. Cyanotic feet. Scar left cav.						+	+	+	+	10	9	0								3	6	III	III	III	III	II b		III	II b	III	II b	Se	—	—
4. Cases of Lupus erythematosus disseminatus (L E D.)																																							
S 28	T. L. 263/55	S. B. ♀ 53	L. E. D. Raynaud's syndrome	10	Scars on ends of 2nd—5th fingers right and 4th left.				2.5	2.5	+		+		10	10	0			4			3		2	1	I f	I f	I c	I c	I c	II b	I c	III	II b	I f	Se		
S 34	M. I. 1018/56	M. E. ♀ 30	L. E. D. Raynaud's syndrome	1	Complaints also in air and warm water.						+	+	+	+	10	2	0						2				I f		I f								Sl		
S 44	T. L. 53/56	M. W. ♀ 34	L. E. D. »Dead fing.»	3/52	Complaints of right hand only.	130/80			3	3.5	+	+	+	+	5	0	0										—	—	—	—	—						Sl		
5. Cases of cold injury																																							
K 1	Priv. 300504	G. R. ♂ 24	St. p. Cold injury	5	No complaints. Cold injury in military service.	110/70			2/100	2.5/90	+	+	+	+	0	0	0	1	1								I a	I b									No		
				5											0	0	1		2		1						I d	I b	I b										
K 2	Priv. 270429	A. R. ♀ 27	St. p. Cold injury	20?	No complaints. Cold injury as child.	130/90			2/120	3/120	+	+	+	+	0	0	0	4										I a	I a		I a		I a				No		
				20?														4														I a		I a	I a	I a			
K 3	Priv. 110321	G. G. ♂ 43	St. p. Cold injury	35?	No complaints. Cold injury as child.	150/100			7/120	7/120	+	+	+	+	0	0	0		5								I b	I b	I b	I b	I b						No		
				36?											0	0	0																						
K 4	Priv. 050918	E. S. ♂ 50	St. p. Cold injury	30	Cold injury in military service	140/100					+	+	+	+	0	0	0	2	1								I a	I b		I a							No		
K 5	Priv. 160908	R. N. ♂ 38	St. p. Cold injury	13	Left thumb and index irritated in cold.	150/90					+	+	+	+	0	0	0		2									I b		I b							Sl		
K 6	M. M. 270525	R. F. ♂ 28	St. p. Cold injury	13	No complaints.	130/80	— 3	293			+	+	+	+	0	0	0																				No		
K 7	Priv. 261218	U. H. ♂ 30	St. p. Cold injury	13	»Dead fingers» in cold.	100/70			3/80	3/80	+	+	+	+	10	0	0																				Sl		
K 8	K. I. 1263/56	K. M. ♂ 16	Cold injury 2nd degree	1/12	Blisters on the ends of right 1st—5th finger, left 4th, 5th.	120/90					+	+	+	+	7	2	0	2								2	I a	—	I a	III	III				—	—	Se	—	

(*Cont.*)

TABLE VIII (*Cont.*)

Series No.	Record No.	Initials Sex Age	Clinical diagnosis	Duration in years	Essential symptoms and signs	Blood pressure syst./diast.	B M R	Serum cholesterol mg/100 ml	Oscillometric index wrist right	Oscillometric index wrist left	Pulse pulpation wrist right rad.	right uln.	left rad.	left uln.	No. of fingers with symptoms	with symptoms and path. reac.	without symptoms with path. reac.	Reactions deviating from the normal. No. of fingers. I a	I b	I c	I d	I e	I f	II a	II b	III	Fingers deviating from the normal range. Distribution of reactions. right hand 1	right hand 2	right hand 3	right hand 4	right hand 5	left hand 1	left hand 2	left hand 3	left hand 4	left hand 5	Character of finger symptoms	Reactive hyperæmia	Ulnar nerve block
K 9	Priv. 080618	M. H. ♀ 47	St. p. cold injury	13	Chronic oedema and chilblains on lower legs.				2/120	3.5/100	+	+	+	+	10	3	0			3							I c						I c	I c			Sl		
K 10	M. P. 4094/55	T. M. ♂ 19	St. p. cold injury 2nd degree	2	Attacks of white fingers in cold air and water.	120/80	−13				+	+	+	+	10	6	0	1		3	3			1			I a	I d	I d		II a		I d	I c	I c	I c	Sl		
				4											10	10	0						10				I f	I f	I f	I f	I f	I f	I f	I f	I f	I f			
6. Cases of neurological disorders																																							
N 1	M. 980505	I. S. ♀ 57	Spondylos. def. cervicalis	6/12	Paresis of right serrat. ant, biceps and triceps brach. Deg. discs $C_V - C_{VII}$.				3.5/130	3.5/130	+	+	+	+	5	0	0										—	—	—	—	—						Sl		
N 2	M. M. 070915	S. N. ♂ 48	Spondylos. def. cervicalis	3/12	Paresis left serrat. ant. and triceps brach. Low pain sensibility ulnar part right hand. Deg. disc $C_V - C_{VI}$.						+	+	+	+	2	2	7						4		5		II b	II b	II b	II b	II b	I f	I f	I f		I f	Sl		
N 3	M. M. 160805	B. B. ♂ 37	Spondylos. def. cervicalis	1/365	Paresis of the left triceps brach. and extensors of the hand. Deg. discs $C_V - C_{VII}$.				3.5/110	4/110	+	+	+	+	5	0	0															—	—	—	—	—	Sl		
N 6	N. K. 241008	G. L. ♂ 32	Right median nerve cut at wrist.	10/12	Paresis in right abd. and opp. pol.-licis. Loss of sens. and persp. in three radial fingers.						+	+	+	+	3	2	0		1							2	I b	III	III								Se	—	
N 7	M. P. I. 6060/55	V. H. ♀ 41	Cervical nerve root affection	7/12	Paresis of the right triceps and finger extensors. Right 4:th and left 2nd finger white and cold.						+	+	+	+	2	2	0						2							I f			I f				Sl		
N 9	T. L. 256/52	H. A. ♂ 31	Postencephalitic state	15	Tremor in right arm and leg. Adie's syndrome. Pain sensitivity decreased in right side of the body.				2.5/90	2.5/90	+	+	+	+	5	5	2	2						1	1	5	III	III	III	III	III	II b	II a	I a		I a	Se		
				15											5	5	1	1					1		1	4	III	III	III	II b	III	I f	I a						
				16 5/12											5	5	3			3						5	III	III	III	III	III	I c	I c			I c		—	+
N 10	M. 030328	H. S. ♀ 52	Spondylos. def. cervicalis	10	Cold, not white hands. Deg. discs $C_{IV} - C_V$, $C_{VIII} - D_I$ Normal arteriogram right arm.	150/95			1.5/100	2.0/100	+		+		5	0	0																				Sl		
N 11	T. L. 187/54	L. J. ♀ 56	Spondylos. def. cervicalis	3/52	Pains in right arm. Slight deg. vert.disc. Cold white right 3rd finger.	160/80			4.5	4	+		+		1	0	0												—								Sl		
N 12	T. L. 136/52	S. A. ♀ 41	Raynaud's syndrome after encephalitis	2	No neurological signs. All fingers cold and white in water. Much improved at second ex.	130/80	− 1				+	+	+	+	10	10	0			2	1	5		2			II a	II a	I d	I c	I c	I e	I e	I e	I e	I e	Sl		
				4											10	1	0	3			1											I d	I a	I a		I a			

TABLE IX.

Series. No.	Record No.	Initials Sex Age	Clinical diagnosis	Duration in years	Essential symptoms and signs: Acidosis	Nephropathy	Retinopathy	Neuropathy	Blood pressure syst./diast.	B M R	Serum cholesterol mg/100 ml	Oscillometrix index wrist: right	left	Pulse palpation, wrist: right rad.	right uln.	left rad.	left uln.	No. of fingers with path. temp. reaction	Kind of insulin administered	Insulin reactions	Control	Reactions deviating from the normal. No. of fingers. I: a	b	c	d	e	f	II: a	b	III	Fingers deviating from the normal range. Distribution of reactions. right hand: 1	2	3	4	5	left hand: 1	2	3	4	5	Character of vascular reaction	Reactive hyperæmia	Ulnar nerve block
1. Duration less than 1 year																																											
D 12	M. 921209	E. E. ♀ 60	Diab. mell. + thyrotoxicosis	3/12	+	—	—	—	110/80	+37	244	5/140	4.5/140	+	+	+	+	0	Z	—	F																					N
										+47								0				4									I a							I a	I a	I a			
D 13	M. 380519	Y. P. ♀ 19	Diab. mell.	7/12	+	—	—	—	110/80	−10	315	2/110	2/100	+	+	+	+	0	Z	—	B																					N
D 14	M. 170514	A. L. ♀ 48	Diab. mell.	1/12	—	—	—	—	150/90	−1	236	2.5/130	2/130	+	+	+	+	0	—	—	F	1									I a										N
				1														0	—																							
D 16	M. 130831	E. K. ♀ 42	Diab. mell.	3/12	+	—	—	—	130/90	−15	263	1.5/90	2.5/100	+	+	+	+	0	Di	—	B		2								I b						I b				N
				5/12						+14								0	Di			1	1								I a						I b				
				10/12														1	Di				2			1					I e					I b	I b				
D 21	M. I. 693/55	H. L. ♂ 25	Diab. mell.	1/12	+	—	—	—	140/70		161			+		+		0	—		G																					N
D 22	M. 290625	J. N. ♀ 27	Diab. mell.	1/12	+	—	—	—	120/80	−7	218			+	+	+	+	0	—	—	B																					N
				3/12														0	N L	—																						
D 24	M. I. 3518/54	S. G. B. ♂ 65	Diab. mell.	4/12	—	—	—	—	125/80		133			+		+		5	NL	—	B			4					1		II b	I c	I c	I c		I c				S
D 25	M. 240605	E. J. ♀ 31	Diab. mell.	6/12	+	—	—	—	140/100	+12	248			+	+	+	+	1	Z		B		1		1						I b	I d								M
D 29	M. 971101	H. L. ♀ 58	Diab. mell. + thyrotoxicos.	1/12	—	—	—	—	210/100	+33	285	5/170	5/170	+	+	+	+	1	—	—	G	1				1										I c		I a			M
D 34	M. I. 1295/55	S. D. ♀ 21	Diab. mell.	3/12	+	—	—	—	145/85		170	3/100	3/120	+		+		0	NL	—	G																					N
D 36	M. M. 970511	K. C. ♀ 58	Diab. mell. + thyrotoxicos.	1/12	+	—	—	+	165/90	+34	235	3.5/150	2/150	+	+	+	+	0	—		G																					N
				7/12				+										7	NL	—				3	1	3					I e	I e	I c	I c	I c	I e			I d	
D 41	M. P. I. 3372/55	Å. M. ♂ 32	Diab. mell.	10/12	+	—	—	—	120/70	−9	260			+		+		0	Z	—	F																					N
D 46	M. M. 051088	E. O. ♀ 50	Diab. mell.	9/12	—	—	—	—	210/110	+14	271	2.5/140	2/130	+	+	+	+	0	—		F																					N
D 56	M. 080121	S. J. ♂ 47	Diab. mell.	1	—	—	—	—	180/100	−10	262	7.5/130	3.5/130	+	+	+	+	5	—		G			5															I c	I c	I c	I c	I c	M
D 57	M. 150418	A. A. ♂ 40	Diab. mell.	1/12	+	—	—	—	150/90	−11	233	7/110	7.5/110	+	+	+	+	1	NL	—	F						1				I f									S
D 58	M. 080630	E. M. ♂ 47	Diab. mell.	1/12	—	—	—	—	170/100	−3	251	3.5/130	3/120	+	+	+	+	0	—		F	4	1								I b		I a			I a			I a	I a	N

(*Cont.*)

TABLE IX. (*Cont.*)

Cases of diabetes mellitus: Series No.	Record No.	Initials Sex Age	Clinical diagnosis	Duration in years	Essential symptoms and signs: Acidosis	Nephropathy	Retinopathy	Neuropathy	Blood pressure syst./diast.	B M R	Serum cholesterol mg/100 ml	Oscillometric index wrist: right	left	Pulse palpation wrist: right rad.	right uln.	left rad.	left uln.	No. of fingers with path. temp. reaction	Kind of insulin administered	Insulin reactions	Control	Reactions deviating from the normal. No. of fingers: I a	I b	I c	I d	I e	I f	II a	II b	III	Fingers deviating from the normal range. Distribution of reactions: right hand 1	right hand 2	right hand 3	right hand 4	right hand 5	left hand 1	left hand 2	left hand 3	left hand 4	left hand 5	Character of vascular reaction	Reactive hyperæmia	Ulnar nerve block
D 75	M. 240501	V. K. ♂ 31	Diab. mell.	1/12	+	—	—	—		—9	233	4/120	3/120	+		+		2	—		B	2		2							I a					I a	I c	I c			M		
D 79	M. I. 180/56	S. M. ♂ 55	Diab. mell. + Alcoholism	8/12	+	—	—	+	120/90	+3	240	1/120	1/120	+	+	+	+	0	Z	—	B	1									I a										N		
D 87	M. I. 459/56	Å. J. ♂ 20	Diab. mell.	3/12	—	—	—	—	130/85	—1	210	1.5/110	1.5/110	+		+		0	—		F	1									I a										N		
D 89	M. I. 676/56	Å. L. ♂ 24	Diab. mell.	2/12	+	—	—	—	115/80	—6	416	2.5/100	2/100	+	+	+	+	0	NL	—	F																				N		
2. Duration 1—5 years.																																											
D 4	M. 240315	A. K. ♂ 30	Diab. mell.	2	+	—	—	—	120/90					+		+		10	Z	—	B					1	1		5	3	II b	II b	I f	I e	III	II b	III	II b	II b	III	S		
D 5	M. 240715	U. Ö. ♂ 30	Diab. mell.	4	+	—	—	—	130/80	+6	203	5/120	5/120	+	+	+	+	10	Ord	—	B			7	1		1		1		II b	I c	I c	I c	I d	I c	I c	I c	I c	I c	S		
				6														0																									
D 10	M. P. I. 2870/55	B. L. ♀ 17	Diab. mell.	4	—	—	—	—	125/85	—13	310			+		+		0	Z	+	F	1									I a										N		
D 18	M. 06 05 20	A. H. ♀ 49	Diab. mell.	2	+	+	+	—	180/100	—6	225	1,5/150	1,5/130	+	+	+	+	10	NL		B								9	1	II b	III	II b	II b	II b	II b	II b	II b	II b	II b	S		
D 30	M. M. 090911	V. B. ♂ 46	Diab. mell.	2	—	—	—	—	110/70	—12	263	5/100	3,5/100	+	+	+	+	10	NL		F						2	2	6		II b	II a	I f	II a	II b	I f	II b	II b	II b	II b	S		
				2 7/12						—3								3										3			II a	II a				II a							
D 40	M. 961126	A. L. ♀ 59	Diab. mell.	5	—	+	—	—	180/100	+12	435			+	+	+	+	2	—		B					1		1							II a			I e			M		
				5 5/12														2					3				2				I f	I f				I b	I b	I b					
D 50	M. 340207	L. A. ♂ 21	Diab. mell.	2	+	+	—	—	110/60			3.5/90	3.5/90	+		+		7	Di	—	F					2	3		2		II b	I e				II b	I f	I f	I f	I e	S		
D 51	M. 310929	C. E. C. ♂ 24	Diab. mell. +thyro-toxicos.	1	+	—	—	—	120/80	+27	159	5/100	5.5/110	+	+	+	+	0	Z	—	B																				N		
				1						+20								0																									
D 53	M. I. 2630/55	L. E. E. ♂ 24	Diab. mell.	4	+	—	—	—	135/80		235	2/120	1.3/120	+		+		3	Z	+	B		1			3					I e		I e		I e					I b	M		
D 64	M. I. 3429/55	V. S. ♂ 43	Diab. mell.	3	—	—	—	+	185/120	—10	345	1.5/150	2.5/150	+		+		1	—		B					1											I e				M		
D 68	M. I. 3529/55	L. B. ♂ 36	Diab. mell.	5	+	—	—	+	135/70		275	2/100	2/100	+		+		3	—		B		1				1		2		II b	I f				II b	I b				S		
D 72	M. M. 050414	A. A. ♂ 50	Diab. mell.	3	+	—	—	—	140/90	+8	315	5/120	5.5/110	+		+		4	—		F					1	1	1	1		II b	II a				I f		I e			S		

(*Cont.*)

TABLE IX. (*Cont.*)

Cases of diabetes mellitus: Series No.	Record No.	Initials Sex Age	Clinical diagnosis	Duration in years	Essential symptoms and signs: Acidosis	Nephropathy	Retinopathy	Neuropathy	Blood pressure syst./diast.	B M R	Serum cholesterol mg/100 ml	Oscillometric index wrist: right	left	Pulse palpation wrist: right rad.	right uln.	left rad.	left uln.	No. of fingers with path. temp. reaction	Kind of insulin administered	Insulin reactions	Control	Reactions deviating from the normal. No. of fingers. I a	I b	I c	I d	I e	I f	II a	II b	III	Fingers deviating from the normal range. Distribution of reactions. right hand 1	right hand 2	right hand 3	right hand 4	right hand 5	left hand 1	left hand 2	left hand 3	left hand 4	left hand 5	Character of vascular reaction	Reactive hyperæmia	Ulnar nerve block
D 81	M. 990930	G. S. ♂ 57	Diab. mell.	4	+	—	+	+	140/90	−28 −13	187	1/110	1/110	+	+	+	+	10	NL	—	B			6		4					I c	I c	I c	I e	I c	I c	I c	I e	I e	I e	M		
D 83	M. I. 262/56	K. E. S. ♂ 49	Diab. mell.	4	—	—	—	+	150/90	− 9	227	1/140	1/140	+		+		9	Z	—	B					1	2		6		II b	II b	II b	II b	II b	II b	I f		I e	I f	S		
				4														7				1				1	3		3		II b	I f		I e	I f	II b	I f	I a		II b		—	—
D 88	M. I. 545/56	L. S. ♂ 19	Diab. mell.	5	—	—	—	—	125/80	+12	182	2.5	2.5	+	+	+	+	0	Di	—	B																				N		
D 95	M. I. 1106/56	G. L. ♂ 45	Diab. mell.	2	+	—	—	+	125/80		280	2/120	2/80	+		+		10	Z	—	B									10	III	III	III	III	III	III	III	III	III	III	S	(+)	
D 98	M. I. 1982/56	B. J. ♂ 16	Diab. mell.	4	+	+	—	—	110/80	−18				+		+		0	NL	—	B																				N		
3. Duration 6—10 years.																																											
D 2	M. P. I. 1964/55	M. R. J. ♀ 23	Diab. mell.	9	+	—	—	—	130/70	−16	175			+		+		0	Z	+	F																				N		
D 3	M. M. 280831	L. I. ♂ 26	Diab. mell. +thyrotox.	10	—	+	—	—	150/90	+32		2/130	2.5/120	+		+		4	Z	—	F	1						2	2		II b	II b				II a	II a	I a			S		
D 6	M. 410702	H. H. ♀ 14	Diab. mell.	10	+	—	—	—	120/80	− 6	225	1.5/110	2/120	+		+		1			B	2				1					I a				I a	I e					M		
D 7	M. 111126	K. W. ♀ 43	Diab. mell. +thyrotox.	6	+	—	—	—	180/120	+26	285	4.5/130	5/140	+	+	+	+	0			F																				N		
D 8	M. 271022	G. J. ♀ 27	Diab. mell.	10	+	+	+	+	105/70	+10	188	1.5/110	1.5/90	+	+	+	+	5	Di	+	B	3		1	1	1		2			I e	II a	I d			I a	II a	I c	I a	I a	M		
				10 6/12														3	·			1		1			2				I f	I f			I a	I c							
				12														0																									
D 9	M. 080417	M. K. ♀ 46	Diab. mell.	10	+	—	—	—	160/90	+17	221	1.5/110	1.5/110	+	+	+	+	10	—		B							1	8	1	II b	II b	II b	II b	II a	II b	III	II b	II b	II b	S		
				10 4/12										10														9	1		II a	II a	II a	II a	II a	II b	II a	II a	II a	II a			
				11														10										8	2		II a	II a	II a	II a	II a	II a	II b	II b	II a	II a			
D 15	M. 250709	S. J. ♂ 30	Diab. mell.	8	+	+	—	+	190/110					+		+		10	Ord	—	B									10	III	III	III	III	III	III	III	III	III	III	S		
D 19	M. P. I. 1859/55	L. G. ♂ 18	Diab. mell.	8	+	—	—	—	115/80	−12	120			+	+	+	+	0	Z	+	G																				N		
D 26	M. I. 779/48	B. W. ♂ 28	Diab. mell.	7	+	—	—	—	125/70	+ 6	238			+		+		2	Z	—	G					2					I e					I e					M		
D 27	M. I. 870/55	B. S. ♀ 23	Diab. mell.	8	+	—	—	—	110/75	+12	145			+		+		3	Z	+	B	2	1			3					I e	I e			I a	I e	I a			I b	M		
				9														0				2										I a					I a						

(*Cont.*)

TABLE IX. *(Cont.)*

Cases of diabetes mellitus																						Reactions deviating from the normal. No. of fingers.									Fingers deviating from the normal range. Distribution of reactions.												
Series No.	Record No.	Initials Sex Age	Clinical diagnosis	Duration in years	Essential symptoms and signs: Acidosis	Nephro-pathy	Retino-pathy	Neuro-pathy	Blood pressure syst./diast.	B M R	Serum cholesterol mg/100 ml	Oscillo-metric index wrist: right	left	Pulse palpation wrist: right rad.	right uln.	left rad.	left uln.	No. of fingers with path. temp. reaction	Kind of insulin administered	Insulin reactions	Control	I a	I b	I c	I d	I e	I f	II a	II b	III	right hand 1	2	3	4	5	left hand 1	2	3	4	5	Character of vascular reaction	Reactive hyperæmia	Ulnar nerve block
D 28	M. I. 1087/55	E. J. ♂ 26	Diab. mell.	9	+	–	+	+	155/100		240			+		+		6	Z	–	F						4		2		II b					I f	I f	I f	I f	II b	S		
D 42	M. 850822	E. A. ♂ 70	Diab. mell.	8	+	+	–	–	170/90	+ 4	255	6/120	6/120	+	+	+	+	1			F						1													I f	S		
D 55	M. I. 106/56	S. S. ♀ 22	Diab. mell.	9	+	–	–	–	110/80	+10	180			+		+		5	Z	+	B						5				I f	I f	I f	I f	I f						S		
D 74	M. I. 3675/55	E. J. ♀ 45	Diab. mell.	10	+	–	+	+	150/90	+33	227	2/100	1.75/100	+		+		0	Z	–	B																				N		
D 82	M. I. 199/56	A. L. ♀ 38	Diab. mell.	9	–	–	+	–	150/100	+13	308	1/120		+	+	+	+	3	Z	–	G	1				3					I a	I e				I e		I e			M		
D 85	M. I. 335/56	A. K. ♀ 56	Diab. mell.	6	–	–	–	–	190/100	+28	385	2/140		+		+		0	Z	–	G		3								I b	I b				I b					N		
D 92	M. I. 840/56	L. A. ♀ 17	Diab. mell.	7	+	–	–	–	130/85	–12	210			+	+	+	+	0	NL	–	B																				N		
D 93	M. I. 904/56	M. J. ♀ 43	Diab. mell.	9	+	–	–	–	130/95		315	4/130	4/120	+		+		0	Z	–	F																				N		
D 96	M. I. 1170/56	L. G. ♀ 17	Diab. mell.	8	+	–	–	–	125/85		210	1/120	1/120	+		+		0	Z	–	B																				N		
D 100	M. I. 1467/56	E. K. ♂ 37	Diab. mell.	9	+	–	+	+	130/85	– 7	285		1.5/100	+		+		10	Z	–	B									10	III	III	III	III	III	III	III	III	III	III	S	—	
4. Duration 11–15 years																																											
D 11	M. 330411	E. J. ♀ 23	Diab. mell.	12	+	+	+	–	190/125	0	293	2.5/160	2/160	+	+	+	+	1	Z	+	B						1					I f									S		
D 17	M. 301109	O. O. ♂ 25	Diab. mell.	14	+	–	–	–	130/80	– 1	263	2/120	2/120	+	+	+	+	1	NL	+	B	2					1				I f					I a				I a	S		
D 20	M. 331115	R. B. ♂ 22	Diab. mell.	11	+	+	+	+	190/110	– 1	187	2/150	2.5/160	+	+	+	(+)		Z	+	B									10	III	III	III	III	III	III	III	III	III	III	S		
				11 1/2																										10	III	III	III	III	III	III	III	III	III	III			
				11 1/2																									5	5	II b	II b	II b	II b	III	II b	III	III	III	III			
				12 1/2																									1	9	II b	III	III	III	III	III	III	III	III	III			
D 23	M. 331229	N. E. T. ♂ 23	Diab. mell.	15	+	+	+	+	160/100	– 5	285	1.5/130	2/130	+	+	+	+	10	Z	+	B							7	3		II b	II b	II a	II a	II a	II b	II a	II a	II a	II a	S		
D 32	M. 100903	I. K. ♀ 45	Diab. mell.	12	+	+	+	+	130/110	– 8	218	3/130	2.5/120	+	+	+	+	10	Z	–	B									10	III	III	III	III	III	III	III	III	III	III	S		
				12 3/12					130/90									10												10	III	III	III	III	III	III	III	III	III	III			
				13														6					1				1		4	1	II b	III	II b	II b	II b	I f				I b			

(Cont.)

TABLE IX. (*Cont.*)

Series No.	Record No.	Initials Sex Age	Clinical diagnosis	Duration in years	Acidosis	Nephropathy	Retinopathy	Neuropathy	Blood pressure syst./diast.	B M R	Serum cholesterol mg/100 ml	Oscillometric index wrist right	Oscillometric index wrist left	Pulse palpation wrist right rad.	right uln.	left rad.	left uln.	No. of fingers with path. temp. reaction	Kind of insulin administered	Insulin reactions	Control	I a	I b	I c	I d	I e	I f	II a	II b	III	right hand 1	right hand 2	right hand 3	right hand 4	right hand 5	left hand 1	left hand 2	left hand 3	left hand 4	left hand 5	Character of vascular reaction	Reactive hyperæmia	Ulnar nerve block
D 39	M. 300515	M. J. ♀ 25	Diab. mell.	13	—	—	—	—	120/80	+ 2	518	1.5/130	1/130	+	+	+	+	0	Z	+	F		1								I b										N		
D 43	M. 250505	I. J. ♀ 31	Diab. mell. Catharact	12	+	+	?	+	215/130	+ 3	255	3.5/150	2/160	+	+	+	+	10	Z	—	B						1			9	III	III	III	III	III	III	III	III	III	I f	S		
D 45	M. P. I. 2580/55	L. J. ♀ 25	Diab. mell.	15	—	—	—	—	115/80	+ 8				+		+		0	—	—	G		1													I b					N		
D 48	M. 210714	S. O. S. ♂ 34	Diab. mell. Catharact	14	+	+	?	+	160/90	+20	248	3.5/120	3/130	+	+	+	+	10	Z	+	B									10	III	III	III	III	III	III	III	III	III	III	S		
D 49	M. 300118	A. J. ♂ 25	Diab. mell.	11	+	—	—	—	135/85	+14	218	3/100	3.5/110	+	+	+	+	0	NL	—	G																				N		
				11 6/12														0																									
D 54	M. I. 3755/55	R. B. ♂ 20	Diab. mell.	14	+	—	+	—	140/100	— 9	265	7/110	6/100	+	+	+	+	0	Di	—	B																				N		
D 62	M. I. 3082/55	M. H. ♀ 35	Diab. mell.	12	—	—	+	+	115/80	+ 8	233	1.5/100		+		+		0	Z	—	G																				N		
D 65	M. I. 14/56	L. L. ♂ 17	Diab. mell.	11	+	+	+	+	150/100	—12	215	1.5/100	1.5/100	+	+	+	+	0	Z	—	B																				N		
D 70	M. I. 3747/55	K. B. ♀ 29	Diab. mell.	15	+	+	+	+	170/115		220			+		+		0	Di	—	B		2														I b	I b			N		
D 76	M. I. 4032/55	R. R. ♀ 45	Diab. mell.	15	+	—	+	—	135/80	+ 4	185	3/120	2/120	+		+		10	Ord	+	B									10	III	III	III	III	III	III	III	III	III	III	S	—	—
D 90	M. 320613	B. P. ♀ 24	Diab. mell.	12	+	—	—	—	135/70	+ 1	233	2.5/90	2.5/90	+	+	+	+	0	Z	—	B	1														I a					N		
				13														0																									
5. Duration 16 years and more.																																											
D 1	M. M. 230311	K. G. ♂ 31	Diab. mell.	24	+	+	+	—	140/100			1.5/140	2/130	+	+	+	+	10	Z	—	F							2	8		II b	II b	IIb	II a	II a	II b	II b	II b	II b	II b	S		
D 31	M. M. 231230	A. L. ♂ 32	Diab. mell.	17	—	—	+	—	120/80	+ 3	233	4.5/120	4.5/120	+	+	+	+	0	Ord	+	G																				N		
				18														0																									
D 33	M. M. 230418	I. F. ♂ 32	Diab. mell.	17	—	+	+	—	120/80	+ 3	230	3.5/120	3/120	+	+	+	+	6	Z	—	B						3		2	1	I f					III	I f	I f	II b	II b	S		
				18														0																									
D 35	M. 201113	R. S. ♂ 35	Diab. mell.	25	—	+	+	+	170/100	+22	263	3.5/140	3/140	+	+	+	+	5	Z	+	B					5						I e				I e	I e	I e		I e	M		
				25														10											3	7	II b	III	III	III	II b	II b	III	III	III	III			
				27														10										2	8		II b	II b	II b	II b	II b	II b	II a	II b	II a	II b		—	
				27 1/2														10											10		II b	II b	II b	II b	II b	II b	II b	II b	II b	II b		—	

(*Cont.*)

TABLE IX. (*Cont.*)

Cases of diabetes mellitus: Series. No.	Record No.	Initials Sex Age	Clinical diagnosis	Duration in years	Essential symptoms and signs: Acidosis	Nephro-pathy	Retino-pathy	Neuro-pathy	Blood pressure syst./diast.	B M R	Serum cholesterol mg/100 ml	Oscillometrix index wrist: right	left	Pulse palpation, wrist: right rad.	right uln.	left rad.	left uln.	No. of fingers with path. temp. reaction	Kind of insulin administered	Insulin reactions	Control	Reactions deviating from the normal. No. of fingers. I a	I b	I c	I d	I e	I f	II a	II b	III	Fingers deviating from the normal range. Distribution of reactions. right hand 1	right hand 2	right hand 3	right hand 4	right hand 5	left hand 1	left hand 2	left hand 3	left hand 4	left hand 5	Character of vascular reaction	Reactive hyperæmia	Ulnar nerve block
D 38	M. 290120	B. F. ♀ 26	Diab. mell.	21	—	+	+	+	130/90	−18	638	1/110	1/100	+	+	+	+	10	Z	+	B									10	III	III	III	III	III	III	III	III	III	III	S		
				22						+2 −7	235							1									1						I f										
D 44	M. 330206	G. E. ♂ 22	Diab. mell.	16	+	+	+	—	160/110	+13	214			+	+	+	+	5	Z	+	B		1	4					1		II b	I c	I c	I c	I c		I b				S		
				16														10						5			5				I f	I f	I f	I c	I c	I f	I c	I c	I c	I f			
D 47	M. 021216	G. M. ♂ 53	Diab. mell. + Anemia perniciosa	20	+	+	+	+	130/70		225	3/150	3.5/150	+	+	+	+	10	Z	+	B						1		8	1	I f	II b	II b	II b	III	II b	II b	II b	II b	II b	S		
				21														10											10		II b	II b	II b	II b	II b	II b	II b	II b	II b	II b		—	
D 52	M. M. 190413	B. B. ♀ 36	Diab. mell.	24	—	—	+	—	190/90	+2		1.5/110	2/100	+	+	+	+	0	Z	—	G																				N		
D 59	M. 040604	H. L. ♂ 51	Diab. mell.	20	—	+	+	+	200/100	+22	232			+		+		3	Z	+	B			1		2					I e	I e				I c					M		
D 60	M. I. 3189/55	S. J. ♂ 44	Diab. mell.	19	—	+	+	+	195/105		818			+		+		10	Z	—	B									10	III	III	III	III	III	III	III	III	III	III	S		
D 61	M. I. 3767/55	L. E. ♀ 30	Diab. mell. Catharact.	18	+	+	?	+	180/130		310	1/150		+		+		3	Z	+	B	1				3					I e				I e	I e	I a				M		
D 63	M. I. 969/56	S. A. ♂ 45	Diab. mell.	18	—	+	+	+	180/100	−23	260	2/110	2/110	+	+	+	+	5	Z	—	F	3		1			1		3		II b	I a	II b	I f	II b			I a	I a	I c	S		
				18 5/12														10												10	III	III	III	III	III	III	III	III	III	III		—	—
D 66	M. I. 3262/55	B. L. ♂ 39	Diab. mell.	28	—	+	+	+	145/85		280		1.25/140	+		+		10	Z	—	F						2		6	2	II b	I f	I f	II b	III	II b	II b	II b	II b	III	S		
D 78	M. I. 27/56	B. G. ♂ 30	Diab. mell.	17	+	+	+	—	160/95					+		+		2	Z	—	F					2					I e					I e					M		
D 80	M. I. 3014/55	S. B. ♂ 26	Diab. mell.	19	—	+	+	+	160/100	+2	180	1.8/140	2.5/140	+		+		0	Z	+	B		1														I b				N		
D 94	M. I. 1083/56	E. S. ♂ 27	Diab. mell.	18	+	—	+	+	120/75	+12				+		+		0	Ord	—	F																				N		
D 97	M. I. 929/56	E. P. ♀ 57	Diab. mell.	16	—	+	+	+	250/110	−24	269	1.5/140	1.5/120	+		+		10	Z	—	F									10	III	III	III	III	III	III	III	III	III	III	S		
				16 3/12														10												10	III	III	III	III	III	III	III	III	III	III		—	
D 99	M. I. 1468/56	G. H. ♀ 39	Diab. mell.	22	+	+	+	+	180/110		395			+	+	+	+	1	Z	—	F	2	2						1		II b	I a			I b		I a				S		

GÖTEBORG
ELANDERS BOKTRYCKERI AKTIEBOLAG
1957